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An Address.[1]

THE CHANGING TREND IN MEDICINE.

By A. D. LAMPHEE,

Retiring President of the South Australian Branch of the British Medical Association.

FIRST of all I want to thank you for the great honour you paid me in having me as your President over the last twelve months. It has been an honour which I have appreciated very deeply, but at the same time it was one which I accepted with some diffidence knowing full well that your President in these days of medico-political controversy needs certain qualities which I lack. However, in my successor I am confident that you will have one who will guide the affairs of the Branch with wisdom and distinction, and I should like to wish Dr. Rieger all the best for his term of office.

These are indeed troublesome and anxious days in which we live. Underneath the thin veneer of apparent prosperity there is an undercurrent of discontent with things as they are, which is apparent not only in the industrial world but in almost every walk of life. There is a growing tendency for people to get as much as they can and give as little as possible in return. We are, in fact, living in an age of revolution, a revolution which has been in progress for the last thirty years at least—one which began gradually and which has flared up into greater activity from time to time and then died down for a year or two.

[1] Read at the annual meeting of the South Australian Branch of the British Medical Association on June 29, 1949.

At present the pendulum is swinging rather violently and many feel that its momentum may land our country in chaos before the steadying hand of wisdom and common sense can still it. It has been a characteristic of every revolution that the community can be roughly divided into three sections. The first comprises the old men who are apt to shake their heads sadly, to say that the country will never be the same again and to sigh for what they call "the good old days". These people always forget that the good old days might have been good and happy and prosperous for them, but were far from being so for a far larger section of the community. They were very much in evidence in opposing reforms in the complacent and prosperous days of Victoria and Edward. The lives of the other people did not concern them; they knew nothing of child labour, the need for prison, asylum and hospital reforms and many cared less.

Another section consists of the young men who have in many cases not had to bear too much responsibility, but who see in the approaching changes a chance to further their altruistic ideas. They are the enthusiasts in every revolution, and they are the ones who give the pendulum its added momentum, rejoicing in the havoc which its added pace causes. Unlike the old men they do not shake their heads and sigh for the good old days, but rather rejoice in the destruction of anything old and traditional and look forward to the new era, when all wrongs will be righted and prosperity will come at the beckoning of a finger.

There is still a large section who, admitting that changes are long overdue, are prepared to cooperate in bringing them about, provided that they are done reasonably and gradually. These are the people whose sobering influence can steady the momentum of the pendulum and so prevent its destructive excesses. They do not receive any support from either the young or the old men, but

the results of the revolutionary change depend largely upon their influence in the community.

There have been revolutions all down the ages, in fact the whole of history is an acount of their influence. Only a few have resulted in bloodshed, of which the French and the Russian are the best examples. In these cases the smouldering fires of discontent had smoked for many years, gradually gathering heat, until only a spark was needed to turn the whole country into a raging inferno. The pendulum gained such momentum that it swept all before it and destroyed everything in its way. Our present revolution has been interrupted by two of the greatest wars in history—wars in which all sections of the community have suffered equally. The old hackneyed phrase "brothers in arms" became very real, especially in the 1939-1945 war. The big homes as well as the cottages were bombed, and there developed in the air-raid shelter a mutual understanding and sympathy between the classes which had never existed before, simply because these people had never had an opportunity of meeting each other on a common level. The same thing happened in the fighting forces. Men and women drawn from all classes of the community came in contact with each other under conditions which encouraged conversation—at first, although they would not admit it, because they were uncomfortable, not altogether happy, and probably desperately worried. In this way deep and lasting friendships have been formed between people who would normally never have met. Included in the friendship is a deep sympathy and understanding of the other fellow's point of view. Tragic as the wars have been, they have served a very useful purpose in giving men and women a more sympathetic understanding of the problems which threaten the life of the community; and I am optimistic enough to think that the experiences gained in war time will increase the numbers and influence of that middle section which, while supporting the need for change, will at the same time put a necessary brake on excesses.

In all times of unrest there is a natural and understandable tendency to worry about the future. The problems of the present and future are apt to fill our thoughts and there is little time or even inclination to ponder over the achievements of the past. Now that the war is over we are already forgetting the glorious history of the rock from which we were hewn. The Battle of Britain and Dunkirk are events which will stir up a feeling of pride in the hearts of all true Britishers for many a long year, and we as Australians have just cause to feel proud of our manhood in Tobruk, Alamein and New Guinea.

In the same way we should be proud of the achievements of our profession. At the present time it is involved in the general progress of the revolution. Here again we have evidence of the existence of the old men who do not want change, the young men who want everything changed, and also of that large stabilizing section who recognize the necessity for change and are prepared to support it wholeheartedly, provided that the results are for the good of the community, and provided that, while gaining what is good in the new, we do not lose forever what has been good in the past. But in thinking so much of the present and of the difficult times ahead, are we not in danger of forgetting altogether what has been done in the past? Do we ever pause to think in these days of new methods of treatment, treatment which is specific and not merely empirical, what the state of things was not so very many years ago. I have in my possession a copy of Reynolds's "System of Medicine" which was published in 1866. The descriptions of the signs and symptoms of many diseases are better than in some modern textbooks, but there are other descriptions, especially in the section on the nervous system, which are difficult to recognize. But when one comes to the portions dealing with ætiology and treatment one realizes that the book was written before the days when bacteriology made such enormous strides and altered our entire conception of the origin of disease. I do not want to bore you with too many examples, but a few are necessary in order to drive home my argument.

In discussing scarlet fever the author writes: "No investigations which have been made into the cause or course of scarlet fever have as yet invalidated in the slightest degree the ancient doctrine that the disease is an effort of nature to eliminate a morbific material."

Malaria is an interesting example of how clinicians were groping in the dark for a cause. The miasm was somehow connected with water, but the high percentage of organic matter was considered the important factor. The writer of the article on malaria states: "Malaria is also generated in hard rocks such as granite in a disintegrating state. A notable example is the island of Hong Kong, which consists entirely of weathered and decaying granite. In such soils, so long as they are undisturbed, the existence of malaria may not be suspected. In the case of Hong Kong, for example, it was not until extensive excavations were made into the disintegrating granite for building purposes that violent and fatal remittent fevers appeared." In the light of our present knowledge how obvious is the answer.

It was also a common belief that water was capable of absorbing malaria and that periodic fevers, dysentery, and even cholera were produced by drinking water so charged. The author is of the opinion that dysentery was caused by miasm, but adds that in the present state of knowledge it is not possible to explain why malaria should in one case cause dysentery and act with intensity on the glandular structures and mucous membranes of the large intestine, and in another excite an intermittent or remittent fever with signs of extreme irritation of the stomach and duodenum going on after to structural changes in those parts. He goes on to state that chemistry may one day reveal to us some difference, at present inappreciable, in the constitution of the miasmata to account for the affinities in the different cases. It is interesting to note that he expresses his entire dissent from the doctrine that "specific agues are the result of suppressed cutaneous secretions under sudden impressions of cold", but he believes the presence of malaria in the blood to be necessary. He wonders, but cannot explain, why the miasmic poison, unlike that of rheumatism or variola or typhus, should produce a periodical and not a continued fever.

It is understandable that typhoid fever should receive a very detailed description. There are various ingenious speculations as to its cause, one of which being the amount of ozone in the air. It was somehow considered to be related to the presence of dunghills, and drinking water becoming contaminated in their vicinity. Filthy emanations from sewers or blocked drains were also thought to be a factor, but the low percentage of cases amongst workers in sewers was rather puzzling. The author admits that the ingestion of putrid animal substances may cause typhoid fever, but then adds that there is nothing more essentially putrid than the decomposed cheese with which many persons habitually indulge their appetites, and that persons unaccustomed to such food can hardly be supposed to partake of it with impunity. Obviously the author was not partial to Gorgonzola!

One could go on quoting for a long time, but these examples will serve to show that only eighty years ago our very able predecessors had no conception of disease being caused by living organisms, and as a corollary they had no ideas at all about prevention. Treatment in those days was, of course, almost entirely empirical and one finds examples of amazing faith in the efficacy of various strange drugs. Quinine and sulphuric acid were indicated for the otorrhœa following scarlet fever. Strong hydrochloric acid mixed with honey was recommended to be applied to the diphtheritic throat, but the author warns that it should not be repeated. The heavy metals were used frequently for different symptoms and strong purgatives, of course, were essential in the treatment of most illnesses. The use of alcohol was strongly advocated, especially wine and spirits. In writing about tetanus the author mentions that he has not much faith in any sedatives, but is far more disposed to administer wine in large quantities than any particular drug—in fact, he considers that ardent spirits undiluted and given boldly might be more efficacious than wine.

If by any chance we who read these accounts should feel inclined to be amused over the ignorance of eighty years ago, we should instead be thankful that we live in days which have been enlightened by the vast knowledge gained by the bacteriologist and pathologist. We should be humbled by the thought that these men had to rely solely upon their clinical acumen and then we can realize that there were giants in those days too.

I doubt, however, whether the advance in medical knowledge has ever been so great and of so much benefit to mankind as in the last thirty years. In this respect medicine has kept pace with the general advance in science, which has altered life entirely during our day. Most of us can remember the first crossing of the English Channel by air, also the first airship. We can remember the introduction of wireless on ships, but I doubt whether in our childhood we ever considered the possibility of such advances being put to such terrible use in time of war. In 1947 Mr. Churchill spoke at a dinner given in connexion with the International Conference of Physicians in London. He said:

> I noted that both John Morley and Edward Grey spoke in 1913 of the advance in science, with unquestioning faith in its wholly beneficent mission. Now, however, when mankind without having improved at all, in fact having lost the sense of many of its most precious values, has got control of the most terrible agencies of destruction and when many of its ablest and most brilliant minds are working night and day on the means of annihilation of the human race—or with portions of it as they may be temporarily opposed to at any time—working on these methods of annihilation both by the devastation of explosives and by the organized spreading of disease among men, cattle and crops. When we look at these manifestations of scientific "progress" it is evident that a certain amount of discrimination must be mingled with our satisfaction at our triumph over nature and of our piercing of her secrets.
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> But tonight our thoughts are turned to healing and not to destruction, and we can unfeignedly and unreservedly rejoice at the progress of medicine and—if I am allowed to mention it here—of its close and friendly companion, surgery. Fanned by the fierce winds of war, medical science and surgical art have advanced unceasingly, hand in hand. The inventive genius of mankind is stirred and spurred by suffering and emergency and the long succession of noble discoveries in the application of the healing art stand forth with all the greater brilliance against the dark and hideous background of hatred and chaos. There is no profession or calling whose members can feel a greater or deeper conviction of duty of lasting value to be done.

Mr. Churchill was right when he said: "Fanned by the fierce winds of war, medical science and art have advanced."

It was in the First World War that blood transfusion came into prominence and the various blood groups became more widely known. This was the start of our present-day system of resuscitation without which no modern hospital could carry on efficiently. The discovery of the clinical value of penicillin was "fanned by the fierce winds of war" and as the result, countless numbers of lives are being saved daily. Enormous strides in the knowledge of malaria and its suppression were made during the war, so much so that it is extremely doubtful whether some campaigns could have been brought to a successful conclusion but for the knowledge gained.

But even without the stimulus of war, medical science during our lifetime has much to its credit. Insulin was first introduced in the treatment of diabetes during my student days, and instead of seeing young diabetics slowly starve until hunger could restrain them no longer and the inevitable breakaway from their diet result in the final coma, we saw a new and normal life open up for them. In my student days it was a common sight to see the well nourished but pale patients with Addison's anæmia. Theirs was the inevitable death sentence, but how different nowadays, thanks to medical science!

We have seen the whole picture of acute lobar pneumonia alter, and also that of the various forms of meningitis and other types of infection, thanks to the sulphanilamides and the antibiotics. I sometimes think that we and the general public are inclined to take all these things for granted, but if we pause to think we should realize that we are living in a remarkable age—an age which surely is capable of further great advances. In view of what has been accomplished since 1866, it is not too much to expect that medical science will unravel the dark and terrible secrets of malignant disease, leuchæmia and other conditions, even in our lifetime.

But what of the future? Let us not be old men and sadly shake our heads and wish for the good old days. Let us rather feel that we are privileged to live in stirring and adventurous days—days of gradual revolution towards the betterment of mankind generally, in which we can, if we act as one body, help to retain the good in the old days. While wisely but firmly restraining the increasing momentum of the pendulum, we should at the same time eagerly grasp what is good in the coming era for the improvement of conditions for the people and to the honour of our profession.

A NOTE ON THE EXTRACTION OF ANTICOAGULANT FROM PERFUSED MAMMALIAN LIVER.

By E. R. TRETHEWIE AND ALLAN J. DAY.[1]

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IN previous papers it was shown that a highly active anticoagulant, possibly a sphingomyelin, was liberated from the perfused liver of the cat (Trethewie, 1945; Trethewie, Cleland and Pengelley, 1947), and in this paper further reports are recorded concerning its purification.

Liver Perfusions.

Under "Nembutal" anæsthesia the livers of five cats (2·0 to 3·2 kilograms in weight) were perfused through the portal vein with heparinized blood taken from the aorta and diluted 1:10 in Tyrode prior to perfusion. The perfusate was collected from the hepatic vein. In the case of each perfusion an amount of unperfused blood was obtained equal to the volume of perfused blood which served as a control in the subsequent extraction. The corresponding diluted specimens of blood from the five cats were mixed to give a volume of 650 millilitres of plasma (unperfused) and the same volume of perfused plasma. These two samples were spun-frozen at −20° C. and then dried *in vacuo* in a serum drying unit. The amount of residue in the case of the perfused (P) was 8·20 grammes, whereas that of the control unperfused (C) was 7·66 grammes.

Extraction of Active Anticoagulant.

The plasma residues were extracted with chloroform-methanol (3:1) in a Soxhlet. Three extractions were made with fresh solvent, each extraction continuing for three to three and a half hours. This gave an extract and a residue, the latter being referred to as "dried plasma residue" and the former as "chloroform-methanol extract". This "chloroform-methanol extract" was stored at −10° C. overnight, when a residue separated. This was denoted as "residue A". The supernatant was concentrated *in vacuo*, and the yellow, greasy, semi-solid residue which separated was collected and labelled "B". To this supernatant (60 millilitres in the case of the control extract and 65 millilitres in the case of the perfused) was added an excess of acetone (six times its bulk), when an immediate white precipitate appeared. It was allowed to stand in the cold for a few days before the precipitate was separated and labelled "C". The precipitate was treated according to the method of Thannhauser *et alii* (1946*a* and 1946*b*) in order to remove the hydrolecithin. A paste was formed by suspending the precipitate "C" in a small amount of water, and this paste

[1] This work was done with the aid of a grant from the National Health and Medical Research Council.

was shaken with excess 0·25 N caustic soda solution at 37° C. for four days. The fatty acids formed were removed by ether extraction after acidification with glacial acetic acid and filtering. The residue after ether extraction was dialysed over running water to remove inorganic constituents, and the "sphingomyelin" was extracted with 3:1 chloroform-methanol. However, the final solution treated with excess acetone yielded no precipitate, so it was concluded either that the active principle was hydrolecithin, or that the active principle had been broken up or otherwise lost during purification or had lost its acetone-insolubility. The mother liquor was not tested for anticoagulant effect.

Since it was possible that had a large amount of active substance been so extracted, the purification might have been successful, another group of five cats were prepared under "Nembutal" anæsthesia and the livers were perfused as before. This time, however, most of the diluted blood was perfused and yielded 1740 millilitres of mixed perfusate. This was shaken in 100 millilitre aliquots with ether and the remaining aqueous layer was then dried *in vacuo* as before. The amount obtained was 14·95 grammes from 1350 millilitres of "ether-extracted plasma". This dried plasma was treated with chloroform-methanol and acetone as described before. The residue "C" obtained was also again treated with caustic soda solution as above, but again no resultant precipitate separated with acetone. The final chloroform-methanol extract treated with excess acetone was evaporated to dryness, and the residue was taken up in Tyrode and tested on cats' blood for anticoagulant properties. The cats' blood was diluted 1:10 in Tyrode and heparin was added to a concentration of 0·012 milligramme per millilitre. To one sample of four millilitres of this diluted heparinized cats' blood was added 0·5 millilitre of the "anticoagulant" solution, and to the other 0·5 millilitre of Tyrode (control). The former developed a trace of clotting in fifty-five minutes, and this did not increase greatly in twenty-four hours, whereas the latter developed a trace in sixty-three minutes, which increased to a large clot in seventy-three minutes and remained so in twenty-four hours. Thus the acetoned final solution still possessed anticoagulant activity.

Further perfusions were carried out and more diluted plasma was obtained from the perfused liver. This was dried and extracted as before (Trethewie, Cleland and Pengelley, 1947). The final sample obtained after treatment of the chloroform-methanol solution with acetone (precipitate) was a greasy, pale yellow material. A few milligrammes of the new extract were taken up in one millilitre of calcium-free Tyrode, and 0·2 millilitre of this was mixed with 0·2 millilitre of oxalated dog plasma and 0·2 millilitre of calcium chloride solution (0·02 molar). Following the addition of thromboplastin (Quick) the clotting times were 295 and 168 seconds. The control plasma similarly mixed with 0·2 millilitre calcium-free Tyrode gave clotting times of 13·9 and 14·0 seconds with thromboplastin (Quick). Thus the extract was very active. Were all the heparin to have passed from the original diluted perfused plasma in the sample thrown down by the acetone, it would have been 12·5 milligrammes. Assay of 0·08 millilitre of the active extract (above) taken up in Tyrode was without effect on toluidine blue in a test (Trethewie and Melvin, 1945) which is sensitive to 0·0025 milligramme heparin (Boots) per millilitre. Though unperfused heparinized control plasma, when extracted by the method described above, after treatment with acetone had previously yielded a substance which had no anticoagulant activity (this indicating that the anticoagulant effect of the perfused plasma could not be due to heparin), this test was carried out because it was thought worth while to determine whether any heparin might come through with this sample. Also in another experiment several milligrammes of heparin were taken up in chloroform-methanol and extracted according to the above procedure; but following treatment with acetone nothing was obtained with activity against toluidine blue which was sensitive to 0·0025 milligramme per millilitre. Further, it is recognized that heparin may have anticoagulant activity and not precipitate toluidine blue; so some of a chloroform-methanol extract which was mixed with heparin and heated in a Soxhlet was evaporated, and the residue was tested and found to be still very active against toluidine blue.

Conclusion.

This work suggests that the anticoagulant is not hydrolecithin and may even be an impurity in the sphingomyelin and not sphingomyelin itself. In view of the alteration of solubility by "partitioning" when organic material is extracted, this latter possibility is being further investigated.

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SOME ASPECTS OF THE PHARMACOLOGY OF MORPHINE, WITH SPECIAL REFERENCE TO ITS ANTAGONISM BY 5-AMINO-ACRIDINE AND OTHER CHEMICALLY RELATED COMPOUNDS.

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DURING the course of experiments designed to give information on the fate of intravenously injected 5-amino-acridine (aminacrin, British Pharmacopœia) it was noted that the experimental animals, which were under surgical anæsthesia with morphine and chloroform, would frequently awaken almost immediately after the injection of aminacrin. A pronounced, but transient, respiratory stimulation was an invariable accompaniment to this phenomenon. A preliminary report of this discovery has already been published (Keogh and Bentley, 1948). This present paper gives a more detailed account of the earlier observations, together with further investigations on the action of a series of compounds related to aminacrin, and some observations on the pharmacology of morphine.

It naturally goes without saying that to test a substance for analeptic activity one must have a narcotized animal as a test object. It was unfortunate for us that of all the laboratory animals, only the dog approaches a lethargic state under morphine, and for our purposes dogs were in short supply. All other animals (and organs) were largely unsuitable for our purposes. However, in the course of our search we did uncover some interesting actions of morphine and aminacrin. In this paper, therefore, the preliminary work is first described, and this description is followed by the more important findings on the dog.

"Monacrin" (Bayer Pharma) was used throughout these experiments. It is 5-amino-acridine hydrochloride monohydrate, and the dosage was calculated on the content of the free base.

THE RABBIT.

Wild Australian rabbits were used as test animals, and the acute toxicity of both morphine and aminacrin was determined. The drugs, dissolved in water, were injected via the marginal vein of the ear.

Aminacrin.

Toxicity determinations with this compound were complicated by the discovery that the lethal dose varied from

one sample of aminacrin to another. However, on that sample which was used throughout, the results were as follows: (i) of a group of 12 rabbits receiving 15 milligrammes per kilogram of body weight, eight were killed; (ii) of a group of six receiving 20 milligrammes per kilogram, five were killed.

Aminacrin, when given intravenously, appears to kill mainly by its cardiac toxicity. The animal which has received a lethal dose is prostrated and weak, and usually exhibits a brief but severe extensor spasm within half to one minute of the injection. Death supervenes rapidly, and if the animal survives for more than three minutes it appears to be out of danger. Immediate autopsy shows the picture of cardiac failure—that is, engorged veins and heart, with occasionally a few weak contractions of the auricle. After death a curious "rippling" of the subcutaneous muscles was often observed. This has also been seen following lethal doses of eserine, and it is interesting to note that both compounds have anticholinesterase properties (to be reported more fully in a later paper).

Rubbo (1947) has drawn attention to the convulsant and excitant action of subcutaneously injected aminacrin in mice. In this case the LD_{50} was 80 millilitres per kilogram of body weight. However, when it was injected intravenously into a rabbit there was no convulsive action, other than that which could be attributed to cerebral anoxia consequent on cardiac failure. One other very pronounced action of aminacrin appeared regularly about fifteen to twenty minutes after the injection, when the rabbits entered a hyperexcitable state, during which the slightest disturbance would elicit symptoms of the most extreme panic. This condition usually lasted for about twenty minutes, after which the animals seemed normal. Whether this is due to some breakdown product of aminacrin or not is still a matter for conjecture.

No chronic toxicity studies were undertaken, since therapeutically only single injections of aminacrin would be needed.

Since intravenously injected aminacrin appeared to kill by a cardiac action this aspect was investigated further, as follows. Rabbits were injected intravenously with a 1% solution of aminacrin until the heart showed the first signs of failure. Those animals which did actually die constituted the series, and the dosage of aminacrin was recorded. In this way an average fatal dose was calculated. It was 17·2 milligrammes per kilogram (seven rabbits). Various attempts were made to diminish this cardiac toxicity, by the use of various compounds, which were injected into the animal either before or after the aminacrin. Amongst these was adrenaline, one to two millilitres of a 1 in 5000 solution being injected intravenously when the first signs of heart failure appeared. In all cases only the most temporary improvement resulted and the animals died during the next ten minutes. Similarly, preliminary injections of digitalin (1·5 milligrammes in each animal) six and a half hours before the aminacrin did not protect the heart, as was the case with morphine (150 milligrammes for each animal) given fifteen minutes before the aminacrin. Since competition had been demonstrated (at least in the case of bacteria) between "Atebrin" and metallic cations, including magnesium (Silverman, 1948), this was tried in the rabbit. Sulphate of magnesium ($MgSO_4.6H_2O$) in a dose of 1·5 millilitres of a 3·5% solution, was given by vein immediately preceding the aminacrin, but no diminution of toxicity resulted. The fact that the injection of magnesium did not protect the heart from the aminacrin suggests that the linking of this drug to the heart muscle is not of an ionic nature, but that the action is due simply to adsorption of the aminacrin onto the heart. If this is true, then there is reason to suppose that the tetrahydro-aminacrin would be less toxic towards the heart, as there is also evidence that it is less readily adsorbed by muscle tissue.

It seems not unlikely that this seemingly high cardiac toxicity of aminacrin results from an idiosyncrasy on the part of the rabbit. This is supported by experiments performed on guinea-pigs, which, while under light ether anæsthesia, received intracardial injections of aminacrin (up to 20 milligrammes per kilogram) without any ill effects other than a temporary cardiac slowing. This solution of aminacrin had been made approximately isotonic with glucose. Solutions stronger than two milligrammes per millilitre, which had not been made isotonic, showed increased toxicity. The isolated frog heart, too, is more resistant to aminacrin and will continue beating in a concentration of 1 in 10,000.

Morphine.

The toxicity of morphine was determined by intravenous injections of the hydrochloride dissolved in water. No corrections were made to allow for the anion. The large quantities of morphine required necessitated the use of solutions approaching saturation. The results were as follows: (i) of a group of eight receiving a dose of 250 milligrammes per kilogram of body weight, one was killed; (ii) of a group of eight receiving 300 milligrammes per kilogram of body weight, four were killed.

Morphine does not kill the rabbit by respiratory depression, but by exhaustion resulting from convulsions and by asphyxia caused by tetanic fixation of the respiratory muscles. This fact has been discussed by Tatum *et alii* (1929). Convulsions appear from thirty minutes to two hours after the injection and strongly resemble strychnine seizures, except that they are more prolonged, lasting up to one hour before death occurs. Opisthotonus, teeth-gnashing, salivation and violent running movements are the most typical symptoms. Little or no narcosis is observed at any stage, and as will be seen from the figures given above, relatively enormous doses of the alkaloid are needed to kill the rabbits. For these reasons it was impossible to detect any clear-cut arousal of a morphinized rabbit when aminacrin was injected. Further, it was not surprising to find that aminacrin, itself a convulsant, did not give protection against morphine convulsions, and in fact usually precipitated typical morphine convulsions sooner than would have been normally expected, and even after subconvulsant doses of morphine (200 milligrammes per kilogram). The only definite sign of antagonism between morphine and aminacrin in the rabbit was provided by the pupil, which was regularly observed to expand from the pinpoint condition caused by morphine after an injection of aminacrin. Now, as was previously mentioned, aminacrin has a strong anticholinesterase action and, were it to act peripherally, one would expect it to cause miosis, as does eserine. The fact that this does not occur in either the normal or the morphinized rabbit points to a central action causing mydriasis.

Salacrin, the 1-methyl derivative of aminacrin, similarly precipitated convulsions in morphinized rabbits. One further interesting point brought out by this work was that, if rabbits are given a preliminary injection of aminacrin (five milligrammes per kilogram—that is, one-third of a toxic dose) and immediately afterwards an injection of morphine (200 to 300 milligrammes per kilogram), typical morphine convulsions may develop at once. In view of this finding it seems unlikely that the convulsant action of morphine is due to the accumulation in the body of oxidation products of the alkaloid, as suggested by McGuigan and Ross (1915).

The Rat.

The rat also was used as a test animal to investigate aminacrin-morphine antagonism. Again this animal was found to be not ideal for the purpose, since morphine produces in it catatonia and only rarely true narcosis. One interesting fact encountered in this work was an apparent tolerance developed by the rat with a most unexpected rapidity. In a group of rats given a dose of morphine sufficient to cause catatonia in all (that is, an intraperitoneal injection of nine milligrammes per kilogram), if immediately after recovery of the whole group the same dose of morphine is given again it will not produce the original action in all the rats, and on the following day the same dose affects even fewer animals. It is difficult to imagine a true tolerance arising so rapidly. It might be suggested that a "competitive inhibition" was being produced between the morphine and its own break-

down products. (Compare Browning and Gulbransen, 1922; Richards and Kueter, 1946.)

Now experiments performed on the dog have shown that intravenously injected aminacrin disappears from the blood-stream at a most surprisingly rapid rate, and preliminary, and admittedly incomplete, investigations indicate that the majority of the drug is bound firmly to the muscles and is rapidly broken down to some bacteriostatically inert compound which is excreted in the urine (Bentley, 1948). Hence it was not surprising to find that intraperitoneal injections of aminacrin produced very little effect on the rat. This fact may also explain the wide discrepancy between the subcutaneous toxicity for mice, as reported by Rubbo, and the intravenous toxicity for rabbits, which is more than five times higher. Now Albert *et alii* (1946) have suggested that bacteriostatic activity in the acridine series is dependent, amongst other things, on a flat molecule. The unexpectedly high toxicity of 1,2,3,4,-tetrahydro-5-amino-acridine when given subcutaneously (Rubbo, 1947) suggested that the "buckling" of the ring consequent on hydrogenation hindered adsorption onto the muscle tissue as well as onto bacteria. Thus when an injection of the tetrahydro-aminacrin was given apparently more of the compound reached the brain than in the case of aminacrin. This surmise was given some support by the finding that intraperitoneally injected tetrahydro-aminacrin was active in the rat. The drug showed an eserine-like action, as would be expected from its powerful anticholinesterase action, and in doses of four to eight milligrammes per kilogram it rapidly abolished both the catatonia and the narcosis caused by morphine (eight rats tested). It must be emphasized that it is a possibility that the abolition of the catatonia results simply from the great muscular weakness caused by the tetrahydro-aminacrin. Light ether anæsthesia temporarily abolishes the catatonia, which returns, however, as soon as the ether effects diminish. However, at least some purely central effect of tetrahydro-aminacrin may be postulated, since the drug rapidly restores the sighting reflexes of morphinized rats.

THE CAT.

In the cat morphine normally causes no narcosis, but a condition usually described as "wildness". From the experience of the authors "acute bewilderment" would better describe the condition, since morphinized cats, while showing both pronounced motor activity and mental confusion, have no trace of aggressiveness whatsoever and make no attempt to bite or scratch when caught. It seemed interesting to investigate the action of aminacrin towards this excitant action of morphine in the cat.

Control Intravenous and Intraperitoneal Injections of Morphine.

It was found that intraperitoneal injections of morphine of up to 20 milligrammes per kilogram invariably caused excitement after a period of about fifteen minutes. The condition was accompanied by dilated pupils and lasted for some hours and then gradually passed away, leaving the animal apparently normal. Intravenous injections, given under local anæsthesia (2% "Novocain" solution), in two cats caused immediate excitement, and in a third cat produced only mild activity. In no case in which morphine was given alone were any convulsions noted (ten cats).

Control Injections (Intravenous and Intraperitoneal) of Aminacrin.

Three cats were given aminacrin intravenously. The saphenous vein was exposed under "Novocain" anæsthesia, and a dose of ten milligrammes per kilogram was injected. This caused immediate weakness and in a minute a brief but sharp convulsive seizure. The animal recovered from this in about one minute, and during the next twenty minutes it seemed panicky and angry, but otherwise normal. Larger doses (15 milligrammes per kilogram) produced severe convulsions.

One cat was given a total of 40 milligrammes per kilogram of aminacrin intraperitoneally in three divided doses. The first two doses (15 milligrammes per kilogram) produced no action, but shortly after the third dose (10 milligrammes per kilogram) the cat commenced mewing and vomited violently. It died some hours later.

Aminacrin in Morphinized Cats.

Intraperitoneal injections of morphine (10 to 20 milligrammes per kilogram) provide in about twenty minutes sufficient analgesia to permit exposure of the saphenous vein without any objection on the part of the cat. In four of the five cats treated in this way intravenous injections of aminacrin (10 milligrammes per kilogram) caused an increase in wildness, which progressed to violent convulsions. Death supervened up to one hour later. The convulsions were accompanied by profuse salivation and widely dilated pupils. The fifth cat in this series showed only the increase in wildness, without convulsions.

Morphine in Cats under Ether Anæsthesia.

The cats were anæsthetized with an ether-chloroform mixture, and a cannula was inserted in the saphenous vein. The morphine was given via the cannula, just as the cats were regaining consciousness. Invariably this produced a deep sleep, without any signs of excitement at all. It is a remarkable fact that whereas morphine alone excites a normal cat, in one just recovering from ether it produces a further and prolonged state of depression. About twenty minutes later the aminacrin was injected. In all, fourteen animals were treated in this way, and of these, seven showed a rapid and pronounced arousal when aminacrin (10 to 15 milligrammes per kilogram) was injected. Of the remainder, two showed signs of arousal. Of those aroused, four developed convulsions and died from one to three hours after the aminacrin injection. One other cat had convulsions, but recovered, and two were killed for other more imperative purposes two hours after the aminacrin injection, but may have developed convulsions had they been left for a longer time. The convulsions could not be controlled by further injections of aminacrin (5 to 10 milligrammes per kilogram), nor by atropine (10 milligrammes per kilogram, given subcutaneously).

Intraperitoneal Injections of Aminacrin in the Morphinized Cat.

No action whatsoever was noted when the aminacrin was given by the intraperitoneal route (two cats).

Comment.

Thus it may be stated that aminacrin potentiates the excitant action of morphine in the cat, and in 60% of the cases studied it was found to have a good analeptic action against the narcosis produced by a combination of ether and chloroform, *plus* morphine given intravenously. A more important observation to emerge from this section of the work was the fact that both in the rabbit and in the cat, a pronounced increase in respiration was noted every time the aminacrin was injected intravenously. This, as well as the work on the dog, has suggested to us the necessity to investigate thoroughly the respiratory stimulant action of aminacrin.

THE DOG.

As long ago as 1874 Claude Bernard (1875) had noted that the dog is the only one of the more usual experimental animals which responds to morphine in a way comparable to the human. He described, too, the vomiting and defæcation which follow subcutaneous injection of the drug, and the mental confusion (fear of humans) and muscular incoordination ("hyenoid gait") which appear on awakening. But the most desirable effect of morphine on the dog, from the point of view of this present work, is the profound sleep which results from the subcutaneous injection of doses of ten milligrammes per kilogram. During this state of depression, which normally lasts for six to twelve hours, it is most unusual for the animal even to attempt to walk when called, tugged by a lead or prodded.

In this series of experiments, the dogs were given subcutaneous injections of ten milligrammes of morphine per

kilogram, which usually produced a deep sleep in fifteen minutes. An occasional resistant individual has been encountered, showing periods of restless walking alternating with periods of sleepiness. However, since it was found that a subsequent repetition of the dose of morphine had but little effect, these resistant animals were not used. In the majority of cases, when the dogs did actually sleep, the analeptic to be tested was administered by intravenous injection, usually via the marginal vein of the ear.

Aminacrin.

In all, ten dogs have been tested with aminacrin. In every case after the injection of five to ten milligrammes per kilogram of aminacrin into a sleeping, morphinized dog, there was an immediate profound but transient stimulation of the respiration. Vigorous defæcation occurred in most cases, and all the dogs awoke within three minutes. Two of them showed nothing more than a greatly increased alertness, and appeared to be well aware of their environment. They did not walk spontaneously, although they would do so if disturbed. The remaining eight dogs all ran about spontaneously, within five minutes of the aminacrin injection. They showed restlessness varying from an almost continuous trotting to a frantic and practically ceaseless running. No relapse to unconsciousness was observed during the period of observation (at least four hours), although the more acutely restless dogs usually became quieter after some time. Both the mental and physical conditions varied from one dog to another, some showing the typical fear and the hyenoid gait of the morphine syndrome, and others appearing almost normal in all respects. The dogs so used were always observed for at least one week after the experiment, and occasionally they have been kept for as long as nine months. No ill effects have been noted. However, salivation was present for about one hour after the injection. This could be controlled by atropine. Since the dog proved so successful a test animal, it was used for "screening" a number of acridines and similar compounds. Those which showed interesting properties were investigated further.

Salacrin-(1-methyl-5-amino-acridine).

Five dogs were treated with salacrin. It behaved similarly to aminacrin, except that the respiratory stimulation was not pronounced. In every case rapid arousal resulted, but the acute restlessness so often seen with aminacrin was not observed.

Proflavine.

Two dogs were tested with proflavine. At a dosage of five milligrammes per kilogram (intravenously), no action whatsoever was noted. A second dog was given twenty milligrammes of the drug per kilogram, with similar completely negative results.

2-Amino-Acridine.

The supply of 2-amino-acridine was limited, and it was not possible to give a morphinized dog more than three milligrammes per kilogram. This produced a mild panic reaction lasting about five minutes. Vigorous defæcation was also noted. After about fifteen minutes the dog relapsed to sleepiness. This compound warrants further trial, in larger doses.

"Rivanol" (2,5,diamino,6-ethoxyacridine lactate).

Four dogs have been tested with "Rivanol". Doses of 10 and 20 milligrammes per kilogram (expressed as milligrammes of the lactate—that is, without correction for the anion) produced only the slightest effect on the morphinized dog. However, when the dose was increased to 40 milligrammes per kilogram, a good arousal was observed. There was none of the frantic restlessness so often observed with aminacrin, nor were there any signs of parasympathetic activity or of respiratory stimulation. On the day following the experiment, both dogs were unusually lively.

This promising result led to toxicity tests in rabbits, which were injected intravenously slowly until the heart commenced to fail. It was found that the average fatal dose was 69·6 milligrammes per kilogram (ten rabbits). This result is in the same range as that reported by Laqueur *et alii* (1924). Thus, "Rivanol" appears to be about four times less toxic than is aminacrin, while for good awakening, eight times as much is needed as for aminacrin.

1,2,3,4,Tetrahydro,5,Amino-Acridine.

Five dogs were treated with 1,2,3,4,tetrahydro,5-amino-acridine, and all showed a rapid arousal from the morphine narcosis, the effect being particularly pronounced in four cases. The respiratory stimulation, too, was noticeable, and was much less transitory than in the case of aminacrin. Profound parasympathetic activity was also shown by this compound.

Unfortunately, tetrahydro-aminacrin, like the majority of related compounds under investigation, was in short supply, and for this reason toxicity tests were not carried out. Rubbo (1947) gives the subcutaneous LD_{50} for mice as 25 milligrammes per kilogram; that is to say, the compound appears to be about three times more toxic than aminacrin. Whether the difference in toxicity would be so great when the compounds were given intravenously is a matter for conjecture.

In the mouse, intraperitoneally injected tetrahydro-aminacrin is very active, doses of five milligrammes per kilogram causing great weakness, generalized muscular twitching, copious diarrhœa, and very deep breathing. This dose did not show any antagonistic action against the effects of three milligrammes of morphine (given intraperitoneally), but did increase the death rate. The three-milligramme dose of morphine, when given alone, killed one out of four mice, but when it was combined with five milligrammes of tetrahydro-aminacrin per kilogram, three mice out of four died.

As was previously mentioned, tetrahydro-aminacrin shows antagonism towards morphine in the rat.

In the rabbit, tetrahydro-aminacrin, in doses of five milligrammes per kilogram, appeared to cause some awakening from the narcosis caused by 200 milligrammes of morphine per kilogram. The respiratory stimulation was pronounced, and no convulsions were observed (three rabbits).

The great power that this compound showed in stimulating respiration led to a trial of its ability to combat the respiratory depression of anæsthetic doses of magnesium salts. It will be remembered that work was quoted earlier (Silverman, 1948) demonstrating antagonism between magnesium and "Atebrin". A dog was given intraperitoneal injections of 4% magnesium chloride solution (a total of 90 millilitres being given during thirty minutes). This produced a condition of drowsiness, and the dog could not be induced to stand. Five milligrammes of tetrahydro-aminacrin per kilogram were then injected intravenously. This dose produced, within one and a half minutes, arousal with the usual panic reaction. The respiration became very deep, and there were the customary symptoms of parasympathetic stimulation. In the guinea-pig which had been given intraperitoneal injections of 5% magnesium chloride solution, to the point of complete anæsthesia and incipient respiratory failure, no clear demonstration of arousal followed the intraperitoneal administration of five milligrammes of tetrahydro-aminacrin per kilogram. However, the respiratory depression was rapidly abolished.

From these results, one may say that tetrahydro-aminacrin displays some interesting properties, and when a further supply becomes available it is hoped to investigate it further.

5-(Ethyl-Amino)-Acridine.

The compound 5-(ethyl-amino)-acridine is the only one in the series in which the amino group is not attached directly to the ring system. It is, in fact, an acridine-substituted aliphatic amine. The small quantities of the drug available made it impossible to test it on more than two dogs. The first morphinized dog received intravenously

five milligrammes of the ethylamino-acridine per kilogram. This caused a most dramatic arousal, with frantic activity which passed in a few minutes into severe extensor spasms of the whole body. These ceased after about three minutes, and the dog then presented a picture of restlessness, with great rage and fear. Considerable bravery was required even to approach the animal for about one hour, after which it became quite docile, and appeared almost normal. On the following day this dog seemed in better health and spirits than is usual after morphine. The second dog, benefiting from the experience gained from the former, received only 2·5 milligrammes of ethylamino-acridine per kilogram. This caused a rapid arousal with panic and great motor activity, lasting at least six hours. Again the dog was very lively on the following day.

5-(Morpholine)-Acridine.

A dose of 2·5 milligrammes of 5-(morpholine)-acridine per kilogram of body weight was injected intravenously into a morphinized dog. Within two minutes powerful tetanic seizures developed. These lasted about thirty minutes. The most interesting feature was that neither during the seizures nor after their cessation was there any sign of arousal whatsoever. The dog continued completely inert for at least six hours, and on the following day was subdued but otherwise well.

Other Chemicals Tested.

The remaining chemicals which were tested were not acridines, but had some points of resemblance to that series.

5-Amino-Quinoline.

The results obtained with one dog suggest a mild and somewhat delayed (about ten minutes) analeptic action of 5-amino-quinoline against morphine.

Tetrahydro-Quinoline.

The intravenous injection of 10 milligrammes of tetrahydro-quinoline per kilogram produced no arousal, respiratory stimulation or symptom of parasympathetic activity in one morphinized dog.

4-Amino-Quinoline.

The compound 4-amino-quinoline derives from aminacrin by the removal of one benzene ring.

Four dogs were used to test the analeptic properties of this substance, which, again, was in short supply. In every case morphinized dogs were rapidly and completely aroused by the intravenous injection of five milligrammes of 4-amino-quinoline per kilogram. The most marked side-effect was the profound respiratory stimulation, which was even more pronounced, though of shorter duration, than that of tetrahydro-aminacrin. Again, parasympathetic activity was observed.

In the rat, intraperitoneal injections of five to ten milligrammes of 4-amino-quinoline per kilogram had no action on the effects of morphine, and when given to the normal rat the drug produced no effects at all. This observation is in keeping with the suggestion that the flat molecules in the acridine and related series are adsorbed readily onto muscle tissue.

Toxicity tests were carried out in the mouse, in order that there should be some basis for comparison of this promising compound with aminacrin. The mice were injected intraperitoneally with a solution of 4-amino-quinoline sulphate, with the following results: (i) when 75 milligrammes per kilogram were given, all four animals in the group survived; (ii) when 100 milligrammes per kilogram were given all four animals in the group died. At a level of 75 milligrammes per kilogram the mice became excitable in about five minutes and showed twitchings of the body. Those receiving 100 milligrammes per kilogram developed violent convulsions after a short time and died ten to twenty-five minutes after the injection. Thus 4-amino-quinoline appears to have about the same toxicity as aminacrin when given intraperitoneally to mice. Insufficient quantities were available for more than a preliminary test of cardiac toxicity, but there is evidence that lightly etherized guinea-pigs will survive 15 milligrammes per kilogram given intracardially.

The high activity of 4-amino-quinoline led to the trial of various derivatives of this compound.

"Nupercaine."

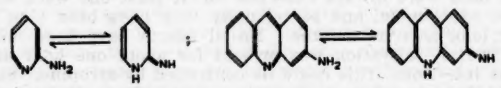
Intravenous injection of five milligrammes of "Nupercaine" per kilogram in a morphinized dog caused a transitory stimulation of the respiration, with cardiac failure in two minutes. The previously mentioned regrettable shortage of dogs has precluded tests on smaller dosage. Later, two milligrammes per kilogram caused convulsions but no arousal.

Quinine.

The intravenous injection of 50 milligrammes of quinine bisulphate per kilogram caused neither arousal nor respiratory stimulation in one morphinized dog.

2-Amino-Pyridine.

The high activity of several compounds having an amino group *para* to a ring nitrogen made it of great interest to test 4-amino-pyridine, which may be regarded as aminacrin lacking both flanking benzene rings. Unfortunately none of this compound was available, and the nearest approach to it was provided by 2-amino-pyridine, which is, in fact, a vinylogous derivative of 2-amino-acridine. This compound probably forms a resonating system between the ring nitrogen and the amino group, comparable with 2-amino-acridine:



The compound 2-amino-pyridine precipitated typical morphine convulsions when given intraperitoneally to morphinized rats or intravenously to morphinized rabbits. When given to normal rats it caused muscular twitchings over the body in a manner reminiscent of tetrahydro-aminacrin.

Altogether four morphinized dogs have received this compound, three by the intravenous route and one intraperitoneally. The dosage ranged from two divided injections of five milligrammes per kilogram each, through eight milligrammes per kilogram to twelve milligrammes per kilogram. In all cases good arousal was noted, with some signs of panic, respiratory stimulation and parasympathetic activity. On the eight milligrammes and twelve milligrammes per kilogram levels strong convulsions developed immediately after the injection and lasted for about five minutes, after which the animals recovered. The dog which was given ten milligrammes per kilogram intraperitoneally showed a gradual awakening, beginning after about ten minutes with salivation and twitchings and continuing through the following half-hour; by that time he would rise to his feet and run on the slightest disturbance.

6-Methyl-2-Amino-Pyridine.

Only one dog was tried with 6-methyl-2-amino-pyridine. It was found that after intravenous injection of five milligrammes per kilogram into a morphinized dog a sharp convulsive seizure developed, lasting about five minutes. The respiration was stimulated, but at the conclusion of the convulsive seizure there was no arousal whatsoever, the dog continuing to sleep for a further five hours.

Amino-Thiazoles.

The chemical similarity of the thiazole ring to the pyridine ring led to the trial of some amino-thiazoles.

The Compound 2-Amino-Thiazole.—Three dogs have been tested with 2-amino-thiazole, which was used at a level of 40 milligrammes per kilogram. Results in this case were somewhat equivocal, but probably point to a mild

analeptic power without panic symptoms and a mild and transitory stimulation of the respiration.

The Compound 2,4,Di-Amino-Thiazole.—At a level of 10 milligrammes per kilogram no arousal of a morphinized dog was noted with 2,4,di-amino-thiazole, but at a level of 60 milligrammes per kilogram (given in divided doses of 20 and 40 milligrammes per kilogram) moderate arousal was noted, with some respiratory stimulation (one dog at each level). The activity of the amino-thiazole suggested the possibility that thiamin might have some antagonism towards morphine. Accordingly a dose of 10 milligrammes per kilogram was given intravenously to a morphinized dog; however, there was not the slightest detectable action.

SPECIFICITY.

It was considered of interest to test the analeptic power of aminacrin against barbiturates, and for this purpose rats were first used. They were given intraperitoneal injections of 40 milligrammes of "Nembutal" per kilogram, and as soon as unconsciousness occurred five milligrammes per kilogram of aminacrin were given by the same route. It was found that the average duration of sleep was not significantly shorter than for the control group. Simultaneous injections of "Nembutal" (40 milligrammes per kilogram) and aminacrin (five milligrammes per kilogram) effected neither the average time of induction nor the duration of the sleep. Further, five milligrammes of aminacrin per kilogram given intraperitoneally five minutes before the injection of the LD_{50} of "Nembutal" did not reduce the death rate.

However, since intraperitoneally administered aminacrin is almost completely without action, other animals with more accessible veins were used. A group of four rabbits was given 40 milligrammes of "Nembutal" per kilogram intraperitoneally. Ten milligrammes of "Monacrin" per kilogram given intravenously had no awakening effect whatsoever. Cats also were used. Three kittens were given 100 milligrammes of "Nembutal" per kilogram intraperitoneally. This caused profound respiratory depression and a subsequent intravenous injection of 10 milligrammes of aminacrin per kilogram caused only the most transitory stimulation of the respiration, after which all three animals promptly ceased breathing and died. Thus it appears that this group of analeptics is quite without action against barbiturates.

SCOPOLAMINE.

One further observation seems of importance. A combination of morphine (10 milligrammes per kilogram) and scopolamine (0·65 milligramme per kilogram) in rabbits has been found to cause a much greater depression than 300 milligrammes of morphine per kilogram alone. Prompt arousal is obtained in these "twilight sleep" rabbits by the injection of five milligrammes of aminacrin per kilogram.

DISCUSSION.

To date the only compounds for which analeptic action against morphine has been claimed are *n*-allyl normorphine and *n*-allyl narcodeine (Hart, 1943). These compounds are said to abolish both the narcosis and the respiratory depression caused by morphine without diminishing the analgesia. It seems fairly reasonable to postulate some competitive inhibition operating between the morphine and the chemically similar antagonists. However, it is difficult to imagine any such mechanism operating in the case of the chemically diverse compounds in this present paper.

One important pharmacological aspect emphasized by the foregoing work is the looseness of the concept of toxicity. Aminacrin (and probably other related compounds), when given subcutaneously, kills by convulsions. But when it is given intravenously the heart is attacked at a much lower concentration. It seems likely that at least some of this effect is due to binding of the compounds to muscle tissue, so that the heart is protected from a sudden high concentration of the compound. The rapid urinary output of the breakdown products of aminacrin (Rentley, 1948) and the delayed appearance of the convulsions suggest that it is not impossible for the convulsions to result from these breakdown products.

The observation that the flat aminacrin is almost entirely without action in the lower dose range when given by routes other than the intravenous, while the "buckled" tetrahydro-aminacrin and the smaller 2-amino-pyridine are both very active when given by these routes, may permit of some cautious predictions of the formulæ of active analeptics having a more prolonged action on the respiratory centre. Amongst these one might include 5,6,7,8,tetrahydro, 4-amino-quinoline, 1,2,3,4,tetrahydro, 5-(ethylamine)-acridine, nuclear substituted derivatives of 4-amino-pyridine, and possibly amino-piperidines. However, up to the present time too few compounds have been tested to provide a basis for correlating structure with activity. The only fact appearing is that an amino group *para* to the ring nitrogen, or possibly in a position where a resonating system may be set up between the ring nitrogen and the amino group, appears essential. On the other hand, proflavine, which does possess this "extra ionic resonance", appears to be inactive, and 5-(ethylamino)-acridine, which has a powerful action, is not capable of forming this resonating system. It is of interest to note that the response of the morphinized dogs to members of the series of compounds investigated may consist of any one, or a combination, of the following phases—respiratory stimulation, convulsions, arousal and excitation. For instance, both 5-morpholine-acridine and 2-amino-6-methyl-acridine produce convulsions without any symptoms of arousal, "Rivanol" produces arousal alone, aminacrin produces respiratory stimulation, arousal and usually excitation (convulsions only on high dosage), while 5-(ethylamino)-acridine develops all four phases of the action. Thus the series may provide useful methods of investigating the many actions of morphine.

Another interesting point arising from the pharmacological investigation is illustrated by the work on the cat. It will be remembered that aminacrin did not antagonize the excitant action of morphine in this animal; in fact, it appeared to potentiate it. It has long been known that morphine has a dual action on the central nervous system, and it is noteworthy to find this duality confirmed through the action of aminacrin. This duality is also demonstrated by the behaviour of the cat towards morphine alone. The alkaloid, when given either intravenously or intraperitoneally, will produce acute bewilderment in this animal; but if the cat has been previously anæsthetized, then only the depressant action is observed—that is, sleep is produced which may be antagonized by aminacrin. This observation may also be considered in the light of the work of Tatum *et alii* (1929). They have stressed the dual action of morphine in all species of animals—that is, a relatively short depressant action and more prolonged stimulation. The gradual wearing off of the depression "exposes" the stimulation. On this basis the withdrawal syndrome is nothing but the "exposure" of long-accumulated excitation. In criticism of this aspect of the theory, however, one might wonder why any depressant drug would not completely alleviate the withdrawal syndrome. On the other hand, some support is lent to the theory by the above-mentioned observation that a cat just recovering from ether or chloroform is sent to sleep by the intravenous injection of morphine. One might assume that the general anæsthetic had rendered insensitive that cerebral centre normally excited by the morphine. If this is so, then aminacrin appears to restore the excitability of this centre. It might be argued, too, in further support of Tatum's conception of the abstinence syndrome, that it would be abolished completely by general anæsthesia; however, as a therapeutic measure this might reasonably be expected to occasion some distaste on the part of the reforming addict.

One criticism of our work might be that we have not shown that a dog will be saved by "Monacrin" *et cetera* from a lethal dose of morphine—we have shown only arousal from narcotic doses. In answer, it is extremely difficult to kill dogs with morphine, and even then death is due to convulsions and not to respiratory failure.

We now believe that sufficient evidence has accumulated from the dog experiments to suggest that a trial of

aminacrin ("Monacrin") and "Rivanol" be made clinically in cases of severe morphine poisoning. A search of the literature reveals no reports of the intravenous administration of aminacrin or its derivatives. On the other hand, "Rivanol" has frequently been administered parenterally (Trautner, 19—) and acriflavine, which appears to be more toxic than aminacrin, has been given intravenously for many years. Assinder (1936) reports giving up to 30 injections of four millilitres of a 2% solution—that is, a total of 2·4 grammes. Acriflavine in the dog has half the toxicity of "Monacrin" but is twice as toxic as "Rivanol" (Heathcote and Urquhart, 1930, Laqueur *et alii*, 1924). Proflavine has also been injected intravenously (Dr. French, private communication), in amounts up to 0·5 gramme daily per patient for a continuous period. Our results show that "Monacrin" has about 140% of the toxicity of proflavine; therefore we consider a single dose of 0·5 to 0·7 gramme to be safe. "Rivanol" is less toxic than proflavine.

In view of these facts it is believed that no undue risk would be attendant on the intravenous injection of either aminacrin ("Monacrin") or "Rivanol". The suggested dosage for humans is as follows: aminacrin, 400 to 500 milligrammes per person; "Rivanol", 1·5 to 2·0 grammes per person. Preliminary medication with atropine would abolish undesirable side-effects, such as diarrhœa and salivation.

Further work has now been commenced with the following aims in view: (i) to find less toxic analeptics; (ii) to find compounds with a more prolonged action on the respiratory centre; (iii) to investigate quantitatively the effect of the analeptics on the analgesia produced by morphine (qualitative observations suggest that the analgesia persists after awakening); (iv) to investigate the effects of the analeptics on the withdrawal syndrome.

SUMMARY.

Various compounds have been investigated for analeptic activity against morphine. They are derivatives of acridine, quinoline, pyridine and thiazole. The most active compounds are aminacrin, tetrahydro-aminacrin, and 4-amino-quinoline. "Rivanol", which is somewhat less active, has the advantage of reduced toxicity. Aminacrin, tetrahydro-aminacrin and 4-amino-quinoline show pronounced respiratory stimulating powers, especially strong in the case of 4-amino-quinoline.

The analeptic compounds have been subjected to a pharmacological investigation, and some aspects of morphine pharmacology have been discussed.

A clinical trial is suggested in cases of severe morphine poisoning.

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ADDENDUM.

As this article was going to press it was decided to try eserine as an analeptic towards morphine. We did this because other work had indicated that some of the analeptics mentioned in the article were powerful anticholinesterases. Out of nine dogs narcotized with morphine eight were aroused by varying doses of eserine, as little as 0·25 milligramme per kilogram given intramuscularly being effective. In this case the arousal was delayed for fifteen to twenty minutes, whilst the arousal with aminacrine was almost immediate. Preliminary experiments with "Prostigmin" indicate that it is not so efficacious. This difference between eserine and "Prostigmin" recalls a similar difference, described by Schweitzer and Wright (1937), in their action on the central nervous system. The dogs after arousal by eserine show marked and persistent weakness and incoordination. Also the animals do not appear so bright intellectually as after "Monacrin".

However, as eserine is a well tried drug, it may be preferable to use it initially rather than "Monacrin"; but the experiments with dogs suggest that larger than ordinary doses may be required. These would be of the order of three to four milligrammes given intramuscularly per person and are the same as those used by Martin and Weiss (1925) in abdominal distension. As all our experiments have been done with animals, and in view of the wide species differences we have encountered, one should not be surprised if the results in man differ somewhat from those obtained with dogs. Accordingly it would be well to try eserine first, and if this is without action to proceed to "Monacrin".

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PELVIMETRY: A REVIEW OF MODERN METHODS.[1]

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THE subject matter which I have been asked to put before you at first appeared to be somewhat complicated; but when I reviewed the modern methods of pelvimetry, I realized that our present-day technique was due to the advancement in radiological equipment rather than to any new or revolutionary method of examination.

The physical laws of radiation still govern all our methods of investigation, but as time and experience have progressed, greater information has been gleaned from the methods which are now used for a radiological pelvic survey. Alexander Orley in 1933 outlined the evolution of X-ray pelvimetry up to that time. His survey is most

[1] A post-graduate lecture, delivered on June 6, 1949, at Brisbane.

interesting, in that he gives 138 references. More interesting still is the fact that Colcher and Sussman (1949) mention that there have been 422 references to the radiological investigation of the pelvis in the past eighteen years.

I must admit that there have been many omissions in my reading and study of the subject, and that the practical application of some of the suggested technical innovations did not appeal to me in many of the articles which I have read. Other articles appeared to be purely radiological in their approach to the subject and seemed to ignore the fact that the radiologist and the obstetrician should work together as a team and that each should appreciate the professional status, the work, and the problems of the other.

From practical experience, and as the result of research in other countries, high-powered radiological equipment and modern devices were developed which simplified many of the technical problems of radiography and allowed the radiologist to come into closer collaboration with the obstetrician. It was inevitable, therefore, that certain teams should evolve and advocate certain methods of pelvimetry and fœtal cephalometry based upon the physical properties of shadow projection.

Unfortunately an X-ray film is not a photograph. If it was, many of the problems with which the radiologist is beset would be solved. It is a shadowgraph which depicts the varying degrees of density of the body tissues, and as such it must follow the physical laws of enlargement and distortion.

All the methods of pelvimetry which have been evolved endeavour to overcome these physical laws in order to obtain a mental or mathematical conception of the true diameters of the bony pelvis and fœtal skull.

Some authors maintain that an attempt to predict the mechanism and course of labour may be made as a result of the visual impression or mathematical results which are obtained from the particular radiological technique which they advocate and employ. The question at once arises: "Are many of these methods universally applicable, and of sufficient accuracy and simplicity to be adopted as a standard method of pelvimetry?" I do not think so, because some of them require considerable individual experience in order to acquire a reasonable accuracy in interpretation; moreover, the actual measurements and their volumetric equivalents may suggest a disproportion which in practice does not exist. These facts may account—in part—for the relatively high Cæsarean section figures in other countries, as compared with Australia.

I will now discuss the various methods of radiological pelvimetry which have led up to our modern pelvic survey.[1]

The method described by Thoms in 1925, and again in 1929, with modifications, still holds pride of place in simplicity of technique, and in the relative accuracy of its bone-to-bone measurements. I have purposely stressed bone-to-bone measurements, because no matter what radiological technique is employed, the X-ray film, or image, is a shadowgraph of the bones comprising the pelvis, the pelvic cavity and the fœtal skull. Many essential factors remain unseen and unpredictable, such as the power and efficiency of the uterine muscle, the laxity or rigidity of the tissues, ligaments and joints of the pelvis, the degree of safe moulding of the fœtal skull, and the slight give-and-take of the living bones in comparison with the dried pelvis and fœtal skull with which one is accustomed to experiment.

Certain authors have declared that their technique, if followed precisely, will give an accuracy of measurement to within a few millimetres. Such a statement tends to omit the unpredictable factors, and seems to assume that all pelves and fœtal skulls are moulded to a similar plan. The Supreme Architect has certainly moulded the pelvis to a plan, but the plan is as variable as the facial appearance of the individual, and has no constant relationship to the habitus of the patient. Similar pelves may be demonstrated in women of totally dissimilar stature, as also may obstetrically dissimilar pelves be demonstrated in women of similar stature. These remarks are made as an introduction to the radiological pelvic survey which I prefer, and which has been adopted at the King George V Memorial Hospital and at the Women's Hospital, Crown Street, Sydney.

I have had no experience with the stereoscopic method of pelvimetry used by the late Dr. W. E. Caldwell and Dr. H. C. Moloy, of New York, because their precision stereoscope has not been made available in this country, and for the reason that I have very limited stereoscopic vision. The method is a personal one and could not be readily acquired by either the radiologist or the obstetrician as a common basis for consultation and study. This appears to be one of its disadvantages.

Twelve years ago I commenced the investigation of a series of cases at the Women's Hospital, Crown Street, Sydney, using the method of pelvimetry and cephalometry described by Ball and Marshbanks. Their method was a comparison between the volume of the fœtal cranium at or near term, with the volume capacity of the pelvis as estimated from the internal conjugate diameter and the biischial diameter. This method was discontinued some time later in favour of a form of pelvic survey. I considered that this method of estimating cranial volume and comparing it with pelvic capacity was unreliable, unless due consideration was given at the same time to the pelvic type so ably discussed and set out by Caldwell and Moloy.

You all realize that a narrow biischial diameter by itself does not necessarily mean an inadequate pelvis at that level; but if the sacro-sciatic notch is long and narrow, the sacrum is inclined forward, and the lateral pelvic walls are convergent, then a narrowed biischial diameter is significant. Again, obstetrically dissimilar pelves may have an equal internal conjugate diameter or biischial diameter, yet it would be wrong to assume that each had a similar volume capacity. For this reason I concluded that the Ball method might lead to the belief that an adequate pelvic cavity might be regarded as inadequate because of a volume capacity estimation based upon a narrowed conjugate or biischial diameter. Such estimations are requested before the onset of labour, and it is not possible in most cases for the radiologist to predict what contribution to the pelvic capacity will be made by the physiologically softened ligaments of the normal sacro-iliac joints and *symphysis pubis*; nor is it possible, before the onset of labour, to immobilize the fœtal head while carrying out the X-ray examination.

The method of Ball and Marshbanks assumed that safe moulding of the fœtal skull would account for a decrease in its volume of an amount up to 150 cubic centimetres. Yet I have seen a well calcified skull, with a volume difference of only 100 cubic centimetres, fail to mould and pass the pelvic brim in a justo-minor mother. The law of averages must play its part, and it is unwise to attempt any standardization based upon volume.

It seems to me that every assessable fact must be duly considered, and that the best method of examination which is available to us at the present time is a general radiological pelvic survey.

The most satisfactory method of eliminating or minimizing enlargement distortion is by teleradiography—that is, by radiography at the maximum practical distance—and the shadow projections should be made in positions which are easily and naturally assumed by the mother.

Three projections only have been found necessary for an adequate pelvic survey: they are an inlet view of the pelvis, an erect lateral view, and a sub-pubic angle view.

Modern high-powered Xray machines, rotating anode X-ray tubes, high-speed screens, films, and Bucky grids, allow films of excellent quality to be obtained at distances greater than four feet; but unfortunately the lack of adequate space for subsidiary equipment in the X-ray departments of both the Women's Hospital and the King George V Hospital at the present time prevents such a technique from being carried out. The equipment at both these hospitals was designed for general radiographic work rather than for specialized procedures. However, I am hopeful that in the near future larger departments with additional equipment will be available.

[1] Dr. Maitland illustrated his remarks with lantern slides.

Accordingly a modification of technique had to be adopted, and for some years now the following pelvic survey has been in use.

The Pelvic-Inlet Film.

The pelvic-inlet film is obtained in the manner of Thoms's pelvimetry, but there are two important variations. The focus film distance is exactly 40 inches (100 centimetres) and the copper plate which is later placed in the exact plane previously occupied by the pelvic inlet is perforated with a pattern of minute holes placed in a series of lines, which are projected on to the less exposed portion of the resultant film. The top line of dots in the pattern are a true centimetre scale from which all the diameters of the pelvic inlet can be measured directly with calipers, just as in Thoms's method. The lower series of dots reproduced by the pattern represent linear centimetre scales at depths of four, five, six, seven, eight and nine centimetres from the plane of the pelvic brim. The plate was mathematically designed for 100 centimetre focus film distance. The depth scales are useful for measuring the biischial diameter direct from the inlet view film, after the depth of the biischial plane has been ascertained from the lateral radiograph. Thus, the type of pelvic inlet and its diameters, together with the measurement of the biischial diameter, can be obtained from the inlet view film.

The exact plane of the pelvic inlet is difficult to ascertain, because of the variations in the height of the promontory of the sacrum; but in general, if the apex of Michaelis's rhomboid and the upper margin of the *symphysis pubis* are parallel to the film, and the shadows of the pubic and ischial bones are superimposed upon the resultant film, then the shadow projection may be considered as being a true projection of the pelvic inlet.

The antero-posterior measurement of the inlet view may vary from the measurement of the internal conjugate diameter as ascertained from the lateral view. It appears to me that there are several factors to account for this in some cases—namely, the variation in the height of the promontory of the sacrum, and the variation in the recumbent position of the patient which is used in the lateral projection in the hospital departments which I attend. Where there is a high promontory, the antero-posterior measurement of the inlet view is a close approximation to the available conjugate as distinct from the true internal conjugate as measured in the lateral view.

The Lateral View of the Pelvis.

Whenever it is possible to do so, the lateral view of the pelvis should be taken with the patient in the erect position, and at the greatest practical focus film distance, in order to minimize distortion. A distance of five feet may be used. Unfortunately, this ideal is not possible in my two small departments, and a compromise had to be made by taking the radiograph with the subject in the recumbent position.

A true lateral view in the recumbent position is more difficult to obtain in a woman because of the wide hips and relatively narrow shoulders. Small pillows are used in order to assist positioning of the patient. The X-ray tube-film distance is limited by the tube-stand to 48 inches, and the central beam of radiation is directed to the upper margin of both trochanters, the shadows of which should be superimposed on the radiograph. A perforated centimetre scale ruler is supported in the sagittal plane, usually in the natal cleft, and the shadow of this ruler acts as a direct measuring scale for all the sagittal diameters of the pelvic cavity, and it also indicates the depth of the biischial plane from the inlet plane, as measured from the tip of the spinous process of the fifth lumbar vertebra and the top of the *symphysis pubis*. This latter measurement allows the appropriate depth scale to be selected on the inlet view pattern in order to measure the biischial diameter directly from the inlet view film. Other facts which may be ascertained from the lateral view are (i) the inclination of the pelvic inlet, (ii) the depth of the pelvic cavity, (iii) the length, shape and curvature of the sacrum, (iv) the presence of sacro-coccygeal fusion and flexion, (v) the shape and size of the sacro-sciatic notch, (vi) the relation of the fœtal head to the pelvic brim, and (vii) the degree of flexion and engagement of the head. This lateral view may be all that is required at term or after commencement of labour.

The inlet view should not be attempted at this stage by those who are unaccustomed to this type of radiographic work, owing to the intensity of radiation which is necessary to obtain a diagnostic radiograph in this position of the patient. The radiologist who is familiar with obstetrical radiography would apply his knowledge of physics, and by the use of high kilovoltage, lower milliamperage, speed screens and increased filtration of his primary beam, he would be able to obtain an inlet view at term with absolute safety to the mother and fœtus. A coarse Potter-Bucky diaphragm is necessary for high kilovoltage work of this type. In general, however, I prefer to carry out a pelvic survey in the earlier stages of pregnancy, as the exposure times are greatly reduced, clear films are obtained from which measurements are made, and the exact positioning of the patient is far easier than in the later stages of pregnancy. Many suspected disproportions at term prove to be unrecognized occipito-posterior presentations.

The Sub-Pubic Angle.

A view of the sub-pubic angle is obtained in the method described by Chassard and Lapiné. The patient sits upon a film cassette, upon which are placed a stationary grid and a perforated centimetre ruler. The patient leans forward until her pubic rami and ischial tuberosities are parallel to the film. Her position resembles that of a cyclist. The X-ray tube to film distance must be at least 40 inches in order to minimize distortion, and the central beam of radiation passes through the ischial tuberosities. When processed the film should clearly show the form and shape of the pubic rami, the sub-pubic angle, and the lateral margins of the obturator foramina.

The sub-pubic angle is measured by drawing tangential lines from the centre of the inferior margin of the *symphysis pubis* to touch the pubic rami at their medial margins. The average sub-pubic angle is 83°. The bituberous diameter is measured by projecting lines along the lateral margins of the obturator foramina to join the tangential lines of the pubic rami. The distance between the points of intersection may be regarded as the bituberous diameter. The lateral obturator lines are a guide to the divergent straight or convergent nature of the pelvic walls, as they approach the outlet. It must be remembered, however, that a narrowed sub-pubic angle, by itself, does not mean an inadequate pelvic outlet, and the pelvis must be viewed as a whole before subnormal aspects can be assessed.

The Fœtal Skull.

I am of the opinion that little relevant information can be given by a routine measurement or volumetric estimation of the fœtal skull, except in the case of a persistent breech presentation, because of the oblique shadow projection of the skull and because we cannot really assess the degree of moulding which will be permissible in one case for the safe delivery of a healthy infant or, in another case, result in a stillborn fœtus.

Conclusion.

I have discussed with you some of the methods of pelvimetry which have led to the present radiological pelvic survey—old methods which have been modified by the advancement of X-ray machines and subsidiary equipment. To dwell too long upon the past is a retrogressive step, and we must look forward to further developments in equipment, rather than confuse the issue with a multiplicity of complicated and time-consuming techniques, graphs, measurements or mathematics.

It is an intriguing thought, for example, to visualize the radiologist of the future "screening" his patients in a bright and well ventilated department while using an adaptation of the television screen coupled to a small, safe, fluoroscopic unit. Indeed, it may be possible, by

the use of a similar appliance, for the obstetrician to observe the actual progress of labour while working in his accustomed surroundings, and, should the need arise, for him to apply forceps and carry out any necessary manœuvre with adequate visual control.

UMBILICUS.

By REG. S. ELLERY,
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To the primitive Asiatic who sat in rapt contemplation of his abdomen, murmuring the sacred word "Om", the navel probably represented the focal point of his universe. But to the modern European this annular relic is merely a pleasant dimple in the flesh, scarcely worthy of consideration even among the most introverted; except that dimples on a woman's body were thought to be the imprints of angels' kisses, and where angels rush in, men need not fear to tread. In olden times the navel was the circle of the sun: it was to the body's microcosm what the sun was to the planetary system; and "Om" was the mystic invocation of the Supreme One. It was the awful word uttered only with bated breath. All things pass away; but to the Indians, "Om" never. It is the symbol of the eternal. The navel marked the place of the womb, the essence of fertility. Vishnu's navel was adored in India, for from it grew a lotus-bud which, when developed, produced the world. The Greek word for navel is ὀμφαλός; and the Greek anchorites, fasting many days and staring with static gaze upon the navel, believed they saw the mystic "Light of Tabor" streaming from this omphalic focus. Tabor itself, a rounded mountain, signified the navel and was thought to be the place where the great light shone when Christ was transfigured. Many years later one of the sects of the Quietists practised contemplation by fixing their eyes upon the navel's mystic knot and thereby stimulated hypnotic reverie. In the sacred cave of Delphi where the temple of Apollo was situated, was a large conical rock which the Greeks called Omphalos or the navel of the earth. "Om" in later times became a talisman; and it is said that the Roman nursemaids used it to prevent their children from being influenced by the demon of the Fascinium. Man and his navel are one; and the little umbilical structure of so scant significance nowadays belongs to the early history of the human race when it figured in the phallic emblems of primitive religion and was concerned with the mysteries of growth and reproduction.

The umbilicus stamps the mark of mortality upon us all. Cain's mark was fixed on his brow; ours is blazoned on our bellies. Large or small, bossed or retracted, it indicates the anatomical centre of gravity and the last link in the embryonic chain. Emperor and clown, gaol-bird and bishop have the same birth-sign and they bear it undiminished to their graves. It sits as prettily upon a prostitute as on the fair belly of a virgin. It dimples the tender skin of the infant and puckers the integument of the aged. Our first parents carried no token of pregnancy; they were without abdominal brand. But many of the gods in the pagan hierarchy were also without umbilication. No midwife clumsily knotted the birth-string of Dionysus, who was born from the thigh of Zeus, nor that of Athene, who sprang from his head. No placenta cumbered the birth of Pandora, who quickened from the clay; and Aphrodite, beauty's paragon, born of the foam, was saved from the cicatrix of her severance.

The navel is phallic only by association. It had a close connexion with generation and the womb. In the prenatal period the site of the navel represented the actual entrance of embryonic life, and therefore became the focus from which the new life evolved. Now it symbolizes the genital passage itself; and in dreams it oftens appears as a vaginal surrogate. Where the early Christian artists, expressing their unconscious wishes, endeavoured to portray the immaculate conception of Jesus, they painted the Eye of Heaven (the sun) smiling upon the Virgin Mary with its radiant beams converging upon her navel. Thus God's essence fertilized the Virgin's womb. Other artists preferred the Virgin's ear as the orifice of divine conjunction, and indicated the Holy Ghost as a dove with its beak in Mary's auricle. Both these ideas originated from earlier pagan cults.

Shakespeare, though he praised the beauty of woman in chromatic words, evidently overlooked the navel. It occurs but once in the whole canon of his works where Coriolanus refers to the touching of the state's navel. Middleton, likewise, used the word in its non-medical manner: "Tis now about the navel of the day", and Massinger, his contemporary, wrote of the body as the navel of a wheel in which rapiers, like spokes, shall meet and fix themselves. Milton and Byron used the word to indicate the unseen centre, the dark, undiscovered middle. Sir Thomas Browne exercised his medical right to use the word umbilicus in his literary works. Little that was beautiful passed unnoticed by Herrick who, in his "Description of a Woman", while apostrophizing her members, notes that

> Where nature in a whiteness without spot
> Hath in the middle tied a Gordian knot.

But, curiously enough, it escaped the notice of Swift when he turned an unclerical eye upon Celia's body in "The Lady's Dressing Room" and proceeded to daub a revolting canvas with excremental smears. In the more sultry climate of the East the body's rapture is more lyrically sung; and the navel has been the subject of poetic comment for thousands of years. In Solomon's Song the Shulamite was beautiful and her navel was "like a round goblet which wanteth not liquor". The large navel was much appreciated by the Eastern people. Women with broad hips and deep-set navels were said to walk with the dignity of elephants. Burton, who translated the "Arabian Nights", says that "a large, hollow navel is looked upon not only as a beauty, but in children it is held as a promise of good growth". The ideal of female beauty in Persia included a navel which would hold an ounce of musk. And the umbilicus of the Hindu maiden is likened to a lotus-bud. But apart from its being a component of beauty, the navel was sometimes regarded as the seat of strength. When God described Behemoth to Job he emphasized that "his force lies in the navel of his belly". Moreover, the fear of the Lord "shall be health to thy navel, and marrow to thy bones". The navel being the embryonic locus of life, it soon signified the hub of social life. London has for some time been the navel of the Empire; just as in the Middle Ages the Crusaders sought to defend Jerusalem because it was then the spiritual omphalos of the Christian world.

Omphalotomy is universally practised; and ingenuity has marked the cutting of the navel-string throughout the ages. Different races have adopted different methods. Some races twist the cord at delivery; some tie it with a vegetable thread or with a hair from the confined woman. Other races cut or crush the cord with a stone or a shell or pierce it with a kangaroo's tooth. In certain places it is rudely torn apart or bitten through with the teeth or nipped with the finger-nails. Custom generally conditions the method and superstition prevents any radical departure. Thus it may be the custom with some tribes to treat the cut ends of the cord with styptics, char them in the flame or apply ceremonial unguents. The retained placenta sets problems to the natives, as it does to modern obstetricians. To certain natives a woman with a retained placenta is regarded as bewitched. Many uncivilized tribes carry out the dangerous practice of pulling on the funis in order to dislodge the placenta. Others, if the placenta appears to be retained, tie the severed end to the mother's big toe; while others fasten a stone to the cut end and make the mother walk about. The ritual of birth extends to the cutting of the cord and magic is often inherent in the procedure. If a child dies at or soon after delivery, it is customary with some tribes to bury the cord with it. Other natives insist on killing the child born with its cord round its neck, lest the child should grow up and kill its parents. Sometimes a piece of bread or a coin is placed under the cord when it is cut. This is supposed to ensure a prosperous life. If the cord is cut upon a

club it augurs that the child will be courageous; whereas if it is done over a stone the future of the child will be sordid and stony. The few inches of cord which sloughs off from the infant's body is a source of ceremony and the seat of magic. Some races treasure this remnant most jealously; while some salt it so that no unpleasant odour will emerge from the child's mouth. In Central Africa the natives place this dried piece of cord in water, believing that if it floats the child is legitimate, but if it sinks the mother is beaten. Omphalomancy, divination from the knots in the cord, was once widely accepted. The number of cord knots was thought to signify the number of future children likely to be borne. Like the animals, probably from conscious mimicry, certain native women, if they wish to conceive again, eat the cords of the children they have just brought forth.

Cord and placenta ritual among the uncivilized is often very complicated and has a deep significance in the life of the tribe. In many instances these contagious magic rites became engrafted upon the tenets of primitive medicine or were believed and practised by the humble and illiterate in Christian countries. The shrivelled residue of a sloughed funis was prized as an effective amulet or charm; and as such it was kept in a secret place or worn round the neck where it preserved life, prevented diseases and banished demons. In powdered form the funis once had wide application in medicine and was administered especially to strengthen the brain. The cord to some was a primitive comforter; and babies when they appeared ill or fractious were given the dried umbilical cord to suck, while the powdered article was long regarded as a potent remedy for children's ailments. Pulverized cord retained its popularity in *materia medica* until comparatively recent times, being especially efficacious in the treatment of epilepsy and chorea. Fresh blood from the umbilicus was thought to cure birthmarks and keloids, and rubbed over the abdomen of the newborn babe was believed to be a good omen and greatly increased the child's faculty for doing good. The inunctions of the present day unfortunately have no moral effect, though they be carried out with righteous hands to the very cadence of praper. Epilepsy, as it is today, has been a therapeutic puzzle throughout the ages. Remedies it has never lacked, but that of Pechey to "anoint the navel with the fat of a cat" must surely be one of the most curious—though less unpleasant than swallowing the afterbirth of a first-born babe or the dung of a badger, and no less effective as a cure for epilepsy than the urine of a faithful wife was for sore eyes. The navel had its uses. Birth-bud of every child, it became significant in the development of the individual and was often anointed to cure some inward complaint or touched with a charm to dispel an evil spirit. Today the doctor regards it with disdain, and the surgeon's interest is aroused only when it becomes herniated. The bifid funis occurs but rarely and excites a merely academic interest. The obstetrician may measure the length of the cord should interest quicken at the sight of an apparent prolongation. Cords of sixty inches have been reported. Umbilical calculi have also been seen, but their significance is of little account. Infantile umbilical hernia is not uncommon, and the adult variety is sometimes seen in persons with pendulous bellies. More than once a pregnant uterus has been found occupying the sac of an umbilical hernia. In other cases the hernia, extending down the *linea alba*, has simulated pregnancy by its size and contour. When the pathology of the abdomen is awry a fistula may develop at the umbilicus, the natal scar discharging pus, urine or gall; and what to the poet's eye seemed a goblet wherein no mingled wine was wanting, then becomes to the surgeon a place of defilement embracing corruption.

Man is not recognized by his navel. Unlike the false prophets in the gospel who were known by their fruits, the navels of men possess a similarity of structure that defies individual discernment, and though they come in sheep's clothing or appear as ravening wolves, the navel shows them to be men, though it does not distinguish one from another. The universal birthmark is indiscriminate; where it formerly excited awe, it now merely entails acceptance. With the passage of years it has lost its news value. It ceases to intrigue. The days of its worship have long passed and no one pays it much regard. It is a cul-de-sac without promise, a dent without design. It affords neither ease nor pleasure. There is apparently no fascination in exposing it and no pervert pays homage to its Asian mysteries. It scarcely constitutes an erogenous zone. But though the fashions of the world pass away and are no longer held in remembrance, the navel remains like a fixed star in the body's firmament, an emblem of birth which cannot be obliterated.

CLINICAL PSYCHIATRY: SOME OVERSEAS OBSERVATIONS.[1]

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INCREASING recognition and interest are being given in the field of clinical psychiatry to the dynamic aspects of personality and to the psychological processes, particularly the unconscious forces which influence and shape behaviour. With the increasing incidence of conflictual situations and experiences, which are universal, the need for emotional guidance becomes greater; consequently greater emphasis is being placed on dynamics, mental mechanisms and psychopathology.

In the United States of America there is a large psychoanalytical school of thought, whose contributions to the understanding of dynamics has been considerable, and the full recognition of a psychodynamic psychiatry is accomplishing much in reducing the distinction between Freudian psychiatrists and non-Freudians to infinitesimal proportions. I do not wish to convey the impression that psychiatry in the United States has been predominantly psychoanalytically influenced; as a matter of fact only one-tenth of the approximately 4500 members of the American Psychiatric Association are out and out psychoanalysts, and I was very impressed with the unbiased manner in which psychiatric problems in that country were being attacked; even in large psychiatric centres where psychoanalytical dominance held sway, any project that held out any promise of getting the patient better was thoroughly explored and all the existing facilities and resources were made available to the investigator. This spirit of scientific cooperation on all sides in an endeavour to ascertain truth creates an atmosphere in such centres the beneficent influence of which is all in the patient's interest and an inspiration to even a casual visitor.

In the application of our knowledge of clinical psychiatry, it is evident that in all countries there is a wide acceptance of the multiplicity of factors which may be involved in any mental illness, and the same desire to arrive at ætiological and dynamic factors in mental illness is evidenced by the type of research that is being conducted into mental illness generally. This can be divided into three categories: work with experimental animals, work with patients from the viewpoint of organic factors, and research from the standpoint of psychogenic factors.

Prolonged Narcosis.

At Brentwood, in England, a good deal of reliance is placed on prolonged narcosis for the reactive and endogenous depressions and late senile depressions, and also for some involutional conditions; "Sodium Amytal" is the drug of choice, the dosage being worked up fairly rapidly. Care has to be exercised to obviate the onset of toxic manifestations, and it is important not to cease the exhibition of the drug suddenly as convulsions may ensue. The patients put on weight and the results in carefully selected cases are claimed to be better than those from electroconvulsive therapy; the method can be usefully applied to patients not responding very well to the latter

[1] Read in expanded form at a meeting of the Australasian Association of Psychiatrists held at Sydney on May 25, 1949.

treatment. Prolonged narcosis may be utilized also as a good method of preparation for shock therapy. It is of great advantage in a modern reception unit, as it permits all new patients, no matter how disturbed or uncooperative, to be admitted immediately for active treatment and ensures a quiet ward with little if any disturbance of other patients.

Favourable therapeutic results have also been claimed from the more drastic use of prolonged "Sodium Amytal" narcosis to produce a toxic drug-delirium, in which the patient not only talks freely but also acts out and abreacts some of his painful repressions (Heldt, 1947), but such methods would appear to be risky in other than experienced hands. Again, "Sodium Amytal" given intravenously in psychosomatic disorders has proved diagnostically valuable; it produces temporary symptomatic improvement, which has, however, to be followed up with further psychotherapy, and it is found to be prognostically of help in determining the depth of a disturbance and its susceptibility to treatment (Canfield, 1947).

Group Psychotherapy and Psychodrama.

I should not omit to mention group psychotherapy and psychodrama, both of which I saw being utilized to advantage in England and America. These, no less than the modern eclectic form of individual psychotherapy, call for considerable resourcefulness on the part of the individual therapist, and he must not only possess intelligence, personality, emotional discipline, judgement and ethical attributes of the highest order, but also be dynamically orientated and thoroughly trained in the necessary techniques and have a sound knowledge of social factors and interpersonal relationships generally. Those whom I saw at work on this method in Washington, District of Columbia, and at the Veterans Administration in Topeka, Kansas, were enthusiastic over the method, and their efforts appeared to be rewarded with promising results.

However, in recalling the discussions on this subject at the International Congress on Mental Health in London, I was impressed with the difficulties that beset even the well trained psychiatrist in this field of therapy.

Group psychotherapy is not so curious as might appear on first acquaintance. It appears to be based primarily on man's natural gregarious instinct to cooperate with others of his own species for survival. We see all around us varied differentiations of this grouping, instances of which are the rebellious, antisocial adolescents hunting in packs, economically depressed or socially disturbed adults in reform groups, or cults such as the nudists or (perhaps more normal in our culture) business men's clubs, lodges or professional associations such as that I have the honour of addressing today. Similar tendencies, patterns of dominance, customs, interaction of personalities and integrations are evident in the dynamics of therapeutic groups. In the therapeutic atmosphere of the group, the hates, jealousies, attitudinal distortions, repressions and what have you are analytically orientated, sublimated or manifested on an inspirational basis, with gradual increasing psychodynamic formulation principally on an interpretative and informative level, so that interactions between members of the group are such as to help them express and understand themselves. The Alcoholics Anonymous movement in the United States of America appears to be a form of group therapy embodying the repressional inspirational approach and expresses the intense relationship developed between the members of the "alcoholics" groups. Apparently in group psychotherapy the patient experiences a sense of value as a member of the group, his self-esteem is raised, and he undergoes desensitization to his difficulties through hearing about similar ones and through recital of his own; a more natural situation is created, in which he can express himself more easily, and through the non-critical, non-hostile acceptance of him by the group he is able to bring up repressed material and also to work through his distorted relationships. The degree or depth of these experiences of the patients in the therapeutic atmosphere of the group is determined largely by the understanding and appreciation of the other members of the group, but also by the skill and interpretations of the psychotherapist. The particular and unique advantages of these forms of therapy open up a further promising field of research in the domain of clinical psychiatry.

So far as psychodrama is concerned, a somewhat different orientation is required to the principles underlying this discipline. Here, in contrast to primarily intrapsychic adjustments, emphasis is placed more on attacking possible problems of adjustment in the patient's environment after his discharge from hospital. Such anticipatory situations are set up by the therapist and acted through by the patient in a protected environment, where the penalty for error or failure is much less traumatic than it would be in the actual situation; the therapeutic atmosphere provides for open constructive criticism under the most favourable conditions, and for the making of suggestions for possible solutions or favourable adaptations when the patient is unsuccessful in working out his own solution.

Group therapy generally has as its object the creation and fostering of healthy emotional attitudes, and its therapy is successful among others in rechannelizing the patient's psychosomatically displaced energies, so that it brings about a catharsis of emotional problems and provides for the release of hostility in a socially acceptable form, the relief of guilt by confession, and the relief of the feeling of isolation by the social interaction of the group.

Group Hypnosis.

I now desire to make an observation on group hypnosis. This method I saw being employed extensively at the Menninger Clinic in Topeka, Kansas. It was quite obvious to me, as a result of my experience of these sessions, that only a psychotherapist thoroughly trained in the necessary techniques should undertake this form of therapy. Group hypnosis, involving four patients at a time, is undertaken to ascertain in the first instance those particular patients who respond sufficiently well to be classified as suitable for this type of therapy. By this means a great deal of the time of the patients' own psychiatrist is saved, as he is helped to avoid attempting to practise a form of therapy that is not likely to meet with success. Time does not permit me to relate the necessary technique in detail, but it is certainly fascinating to behold—the visiting psychiatrist both seeing and hearing the whole procedure through a two-way mirror, himself unbeholden and unknown to the patients concerned. I am satisfied that this form of therapy in competent hands should find a place in any modern psychiatric programme.

Ether Abreaction.

Ether abreaction was found mainly at special centres, either psychiatric sections of general hospitals, such as Saint Bartholomew's, London, or at naval or military establishments. The technique is no doubt well known to you and needs no elaboration by me. Its value in the treatment of certain traumatic emotional illnesses has been fairly firmly established, although it has a limited field of application.

A Pharmacodynamic Treatment of the Psychoneuroses.

Some brief observations might now be recorded on a pharmacodynamic treatment of the psychoneuroses. While at the Illinois Neuro-Psychiatric Institute in Chicago, I had an interesting discussion with L. J. Meduna on his recent investigations of the effects of gas inhalations on the psychoneuroses, and I am indebted to him for the following account of the method. Meduna is using a mixture of carbon dioxide and oxygen, and states that the beneficial effects of convulsive treatments depend on the agent used only in so far as the particular agent, mechanical or electrical, produces convulsions of the *grand mal* type,—that is, cortical in origin. Epileptogenic agents, producing motor but not cortical discharges, seem to have no curative effects on psychotic conditions. This is possibly due to the fact that mental disorders (schizophrenias, schizophreniform states, melancholias *et cetera*) are disturbances of cortical functions—that is, higher associative functions. Unlike psychoses, the psychoneuroses may be conceived of as disturbances of lower

structures of the brain, which upset or distort the emotional values of concepts.

Consequently, a search was made for a method which would affect mainly the lower structures of the brain, with the possibility of effecting a profound alteration of the pathological symptom in the psychoneuroses. This method of gas inhalation has the unique feature of a direct attack upon some neurotic symptoms without the help of any so-called psychotherapy. Thus recovery depends entirely on the effect of the gas upon the brain tissues of the patient.

I have made arrangements for this new form of treatment to be introduced at Broughton Hall. An inhalation mask with a central valve has been utilized, and I had made provision for the inclusion of a humidifying bottle in the gas circuit, but we have not included this to date. The patient is told that his malady or trouble is considered to be nervous in nature, and that for it he will be subjected to an inhalation treatment. He is told that the gas to be inhaled will produce a particular kind of anæsthesia, during which he may experience unusual dreams, emotions or thoughts. These experiences may or may not be important, but he is encouraged to relate any that he remembers on awakening. Timid patients may have to be reassured as to the safety of the treatment. In order to minimize the suggestive element in the treatment, the patient can be told that one cannot know in advance whether the treatment will help him.

Physiological Reactions.

The physiological reactions follow a definite pattern in the following order: (i) subcortical excitation; (ii) cortical inhibition; (iii) psychomotor and psychosensory excitation, possibly by the stimulated subcortical structures; (iv) extrapyramidal and other motor phenomena and subcortical epileptiform attacks.

As a rule, the extrapyramidal symptoms appear around or beyond the thirtieth respiration. The first signs are slight tremor, tetanoid spasms of the hands and later in the face or trunk, athetoid movements and ballism; rigidity develops first in the flexor and later in the extensor muscles, and then the Babinsky sign or a continuous Babinsky position of the big toes appears. By further continuation of the respiration of carbon dioxide, one may produce signs of decerebrate rigidity and—upon resumption of respiration of room air—epileptiform attacks; these differ from the cortical convulsions of the "Metrazol" and electric shock treatments, and are of limited therapeutic use.

It can be said that the patients are free from any danger of tongue-biting, fracture or dislocation; they do not urinate or defæcate.

Mode of Action.

Clinical improvement in psychoneuroses is attained in one of the following four ways:

1. Simple diminution and disappearance of the symptoms. Patients improving in this way received no more than 15 to 25 respirations during each treatment; they required a course of 40 to 100 treatments.

2. Direct abreaction of pathogenic emotions. Patients in this group received from 15 to 40 respirations at every treatment. The reaction of these patients is extremely dramatic; they live through their pathogenic experiences again and again, and discharge their emotions, sometimes with great force. For instance, Meduna quotes the case of one patient, a young woman, who had been raped twice in her life and who suffered from an anxiety neurosis; she relived the attempts at rape, fought and kicked violently, screamed, crossed her legs and defended herself vigorously during the awakening phase; the psychomotor reaction diminished as the patient improved.

3. Indirect abreaction. By this term is meant the phenomenon of discharging pathological emotions or feelings, not through revival of past pathogenic experiences, but in connexion with symbolic dreams.

4. Spontaneous analysis and reintegration to a more normal personality pattern. Patients in this group do not show any considerable emotional discharge and may or may not have a symbolic dream or a dreamy recollection of some past experience during the treatment. However, later during the day the patients recollect forgotten or suppressed childhood memories, or other pathogenic experiences, and discover their causal relation to the actual symptoms. As the treatment proceeds, more and more of this material is revived by the patients and the pathological symptoms correspondingly decrease or disappear. Patients belonging to this group received from 20 to 30 respirations. The longest course of treatment, from 70 to 120 treatments, is needed for patients in this group.

Indications for the Treatment.

So far as indications are concerned, when we take into consideration the difficulty of making any adequate classification for the psychoneuroses, it can be said that almost all the patients with conversion symptoms, such as those who create physical symptoms without underlying organic abnormality or those who create pseudo-psychotic symptoms, are easily manageable by the inhalations. Also, those patients with faulty control of emergency reactions, with symptoms of sense of guilt or of inadequacy, and with irritability and anxiety neuroses, are suitable for this type of treatment. Patients with personality maladjustments, manifested by asocial and unconventional behaviour and emotional instability as well, benefit from this procedure.

The treatment is of no avail in the anakastic reactions, such as the obsessive and compulsive neuroses, and the so-called neurasthenic syndromes, fatigue, general weakness and hypochondriacal neuroses, are not influenced permanently by the treatment. So far as any psychotic conditions are concerned, the treatment can be regarded as only transitory in nature.

Contraindication.

The only definite contraindications for the treatment that are known of are "open" tuberculosis of the lungs, high blood pressure, and organic heart disease.

Discussion.

It is quite possible that the results of this treatment could be greatly improved if it was supplemented by psychotherapy, but it is proposed in the introduction of this treatment at Broughton Hall to eliminate psychotherapeutic measures in conjunction with the treatment in the first instance, to ascertain definitely if this pharmacodynamic treatment, in its direct approach to the deep structures of the nervous system, can be definitely differentiated in its results from the psychological forms of therapy. After such experimental approach, consideration will, of course, be given to supplementing of the treatment with psychotherapeutic procedures.

Insulin Coma.

There appeared to be a considerable amount of variation in the application of therapeutic techniques so far as insulin coma was concerned. At Bethlem, and in fact at most of the large centres utilizing to any extent this form of therapy, courses of deep insulin coma were regarded as most satisfactory, particularly for the more malignant conditions, the methods set out by Sargant and Slater (1944) being largely followed. Insulin shock treatment combined with other psychiatric procedures would appear to be the best treatment for patients suffering from schizophrenia; it, of course, requires special facilities and additional staff, as well as special nursing care, but it would appear eminently desirable from several points of view to continue the use of this procedure at the sacrifice of other facilities in many cases. Insulin treatment, if given during the first six months of the disease, will produce remissions in three cases out of five, although the proportion of remissions declines to 25% or less when the disease has existed for two or three years; there is no doubt, however, that it is preeminently the method of choice for these patients, who occupy about half the total number of beds in our mental hospitals. In some chronic cases there is an absolute resistance to insulin, some of

the patients showing no pronounced reaction even to very high doses, and in many cases this could be regarded as prognostically significant. In some cases the effect of the treatment is simply to change the clinical picture without affecting the basic disease. The paranoid types of condition appear to represent the more superficial physiological disturbances and the catatonic types the more profound disturbances; again, florid symptoms, so far as they indicate an acute process, seem to be prognostically more favourable than bland and chronic symptoms which have imbedded themselves more deeply in the patient's personality.

The nature and the mechanism of the schizophrenics' reaction to hypoglycæmia remain a mystery at the present time. However, I was privileged to have a full afternoon's discussion with Professor McCulloch of the Neuro-Psychiatric Institute of the University of Illinois, and was most interested to follow the lines of some of his research on the chemistry and metabolism of the brain generally. His brilliant work along such lines will, I feel sure, do much to elucidate for us some if not all of the aforementioned mysteries. Different subjects vary a great deal in their susceptibility and response to similar doses of insulin, and the effects of low blood sugar levels vary widely in different people. This may all be wrapped up with the constitutional capacity of the particular individual's brain to utilize carbohydrate or carry out oxidative processes and possibly with the liability or otherwise to damage of the walls of the cerebral capillaries, producing an increased permeability with various types of hæmorrhage or œdema.

A modified method of its use has given good results with asthmatics. Here anxiety is relieved as in cases of frank psychoses, in which with the relief of anxiety the psychotic manifestations are often rapidly dissipated. Here, of course, as in other forms of therapy, organized psychotherapy can be combined with advantage.

Chemical Shock.

The chemical shock method, or as it is more commonly called, the "Metrazol" convulsion method, advocated by Meduna in 1934, has been almost universally replaced by the electroshock convulsive method introduced by Cerletti and Bini in 1938. The advantages of the latter method over the former are well known to you: it is the least complicated in its execution, the patients are amnesic for the treatment, and the anxiety experienced in connexion with it is much less in evidence. However, I personally still believe that in some cases of schizophrenia, particularly with catatonic patients who have had a sudden onset of symptoms, more favourable and more lasting clinical remissions can be expected with chemical shock than with any of the electroconvulsive methods.

Electroconvulsive Therapy.

Some relatively recent modifications in the technique of inducing electroconvulsive shock have been introduced in England and America, but I saw no evidence of these methods being exploited or investigated on the Continent; in fact in France and Switzerland the types of apparatus being used were outmoded and outdated in comparison with those in England and the United States of America. A considerable improvement in the technique of the administration of the ordinary raw current was the adoption of a *glissando* in the electrical circuit instead of the usual mass condenser discharge. In the American instruments this unit functioned automatically over a given period of time, but in the English instruments the result was generally effected by a manually controlled rheostat, a quick turn of which raised the amperage from 0 to 200 milliamperes, or more if desired. In this way the patient received the dosage in an ascending order of intensity instead of in a mass discharge, and there is no doubt that the severity of the tonic stage of the convulsion is lessened and the response to the stimulus runs more smoothly, in place of the often sudden, violent onset with consequent greater liability of the patient to fractures.

In ordinary electroconvulsive therapy the number and spacing of treatments vary from case to case, but the usual average appears to be three a week. In some centres, however, particularly Portsmouth in England and Chicago in the United States of America, the intensive method is adopted and as many as four treatments a day are given, the dosage being modified according to the patients' response to treatment; in some cases the patient is reduced to the infantile level, in which he is quite helpless and doubly incontinent. During the patient's emergence from the confusional state psychotherapy is given and later occupational therapy is included as an adjuvant. In a series of 100 cases at Portsmouth, made up of anxiety states, hysteria and obsessional and mixed states, 51% of the patients were classified as recovered, 46% as relieved and 3% as not improved. The procedure was claimed to be especially suitable in chronic cases, and no prolonged memory defects were detected in any of the patients so treated.

A further modification of the use of the raw current was one I saw in use at Saint Bartholomew's Hospital, London. This was known as the steep wave type of convulsion. Strauss and MacPhail, the originators of this type of current, thought that with it the cellular cerebral structures would be less affected and that the excessive physiological excitation experienced with the ordinary sinusoidal type of current might be avoided. The rapid change in interelectrode resistance during the first few impulses of the shock current indicated to them the desirability of using a rapidly damped train of waves, the higher voltages at the beginning overcoming the initial resistance and the subsequent decrement ensuring that minimal energy was used to induce the fit. This type of instrument utilizes a condenser discharge, the pulse waves being monophasically or diphasically directed. The diphasic wave form is said to produce more intracellular disturbance than does the monophasic.

The monophasic current is said to produce slightly less confusion and to make for a quicker recovery, while the diphasic ensures a major reaction in subjects who are agitated and very restless, or if for any reason difficulties in making good contact are encountered. The indications for this type of convulsive therapy differ in no way from those already being provided for by the ordinary standard type of equipment, and the clinical results are identical. With this method it is claimed that the convulsions are less violent and of shorter duration, and recovery from the fit is more tranquil and rapid.

While at Saint Bartholomew's in London I had the opportunity of seeing a further development of this form of therapy in what has been termed electronarcosis or electrocoma. Personally I think the term is misleading, as the condition induced is essentially not a true coma, but a form of exhaustion due to excessive overstimulation of the central nervous system as a whole. At "Bart's" the patient is first made to have a convulsion by means of the steep-wave type of apparatus just previously described, the dial being set at 15 to 18 joules, and after an interval of two or three seconds only is switched over to an apparatus known as the pulsicon, which delivers a pulse wave of low frequency with regularly placed intervals and amplitude. This current is constant and is passed continuously for a period of seven or eight minutes, but it can be regulated by means of a manual rheostat.

This method of electroplexy, as I prefer to call it, necessitates some premedication of the patient: a quick-acting barbiturate may be administered, but preferably 0·3 to 0·5 gramme of "Pentothal" or "Sodium Amytal" given intravenously. One-sixtieth of a grain of atropine is given through the same needle; it inhibits perspiration and excessive salivation and also prevents cardiac and respiratory inhibition from overaction of the vagus nerve. If the use of curare is indicated, it can be given after the "Pentothal" through the same needle from a different syringe. Treatment is commenced three or four minutes after such premedication; "Carbogen" or pure oxygen is administered throughout the whole treatment. The method adopted here calls for expert teamwork: an anæsthetist, a physician to record the pulse at minute intervals, a physician to record the blood pressure and a physician to control the apparatus and dosage, together with trained

nursing assistance for attention to details of application of the treatment.

With the Shotter-Rich type of apparatus favoured in many of the leading centres in England, the current is gradually raised from zero to 200 milliamperes or less in the course of about half a second, replacing the sudden violent stimulus to the brain from a relatively high current. This current passes for several seconds according to the level of amperage and is then abruptly reduced to about 70 milliamperes or lower until the patient starts to breathe. It will be observed in this method that the clonic movements are less violent, because agonists and antagonists are still in a state of increased tonus and injuries or fractures are most unlikely. When respiration is well established, usually during the beginning of the second minute of treatment, the degree of electroplexy desired can then be obtained by raising the milliamperage gradually at the rate of five every fifteen to twenty seconds, depending on the character of the patient's respiration, but as soon as stridor occurs the current should be advanced no further or kept slightly below that point; the degree of tonicity can be detected by flexing and extending the patient's forearm. The nature of the respiration and clonic movements will depend on the nature of the premedication, if any—that is, either barbiturate or curare. When the pronounced clonic movements occur, respiration generally begins immediately after they end. The gag is removed, the airway is passed, suction catheters are placed in appropriate positions, and the "Carbogen" mask is then placed over the nose and mouth, "Carbogen" being supplied at an approximate rate of 12 to 15 litres per minute. Sometimes a certain amount of respiratory distress, prolonged cyanosis or pronounced laryngeal stridor occurs when the maintenance current is kept at too low a level; this may be overcome by placing the electrodes in a slightly more anterior position. The variations in patients' reactions, indicating a raising or lowering of the current either in individual or subsequent treatments, and knowledge of the correct degree of maintenance current, are naturally acquired by the psychiatrist after adequate experience of the technical aspects of the treatment. A good degree of tonicity, with some flexion at the elbows and a slight degree of respiratory stridor, indicates that the correct level of maintenance current has been reached.

Although one rarely hesitates to employ ordinary straight-forward electroshock therapy in cases of hypertension, clinical experiences with this type of therapy would appear to justify hypertension's being regarded as a definite contraindication. The initial cardiac arrest followed by bradycardia is attributed to vagal stimulation; the tachycardia and hypertension which develop later to stimulation of the sympathetic system. At the Portsmouth centre in England, enthusiastic claims are being made for this form of therapy in cases of schizophrenia, but the same results have not been achieved elsewhere. In Switzerland it is generally regarded unfavourably and in the United States of America with a good deal of doubt as to its being a more favourable or worthwhile method of treatment. I think that it is reasonable and accurate to summarize my experiences of this therapy by saying that it is still undergoing extensive clinical trial and certainly cannot be regarded or accepted as an established form of treatment of the psychoses or psychoneuroses.

The use of curare in electroshock therapy requires a short observation. This drug in one or other of its compounds in therapeutic doses effectively blocks transmission of impulses across the myo-neural junctions of voluntary muscle, consequently producing temporary but good muscular relaxation, and its evanescent action due to rapid elimination in such doses renders it non-toxic to the patient. In England it is used largely in the form of "Tubocurarine Chloride". At the Johns Hopkins Hospital, Baltimore, Squibb's "Intocostrin" is used as a routine agent; here as a precautionary measure they always use three-quarters of the standard dose recommended and have never had any trouble with such doses. At Munsingin, Berne, Switzerland, they also favour "Intocostrin", as with the English preparation they experienced paralysis of the diaphragm in some cases. With properly graded doses oxygen administration is not required, but it should be at hand for use in the event of respiratory embarrassment. "Intocostrin" is administered as a uniformly sustained intravenous injection over a period of sixty to ninety seconds in a dose of half a unit per pound of body weight two to three minutes before the shock is given. The initial adult dose should be 20 units less than the total therapeutic dose worked out on the basis of body weight. At Munsingin they follow the injection of "Intocostrin" with "Prostigmin" (Roche) 1:2000 in a dose of one millilitre and immediately afterwards give the shock. If the intramuscular route is used the dose requires to be increased in both cases. The "Intocostrin" is given first, and some ten to fifteen minutes later the "Prostigmin", which is then followed by the shock. This permits of the action of the "Prostigmin" being brought into play without any delay and as soon as the physiological effect of the "Intocostrin" has been advantageously utilized and is no longer necessary. Great care should be exercised in excluding *myasthenia gravis* from the clinical picture, as this condition is dangerously sensitive to the drug. Pulmonary disorders, disease of the liver and renal dysfunction are also definite contraindications. At La Waldau, Berne, they are replacing curare with the preparation "Parpanit".

I might here interpolate a few remarks on the possibility of occurrence of neuropathological changes in the cerebral tissues as a result of electroconvulsive shock; a considerable amount of research has been and is still being carried out abroad in an attempt to satisfy this query. A very careful scientific and critical consideration of the results is required before any definite conclusions are reached in the matter, particularly in relation to experimental animals and such laboratory animals as are used as controls. At the Veterans Administration Hospital, Topeka, Kansas, air encephalograms have been prepared in several cases, and in three-monthly follow-up studies in some cases enlargement of the ventricular system has been found; but that may not have any direct relation to the treatment, and they are not convinced that they have demonstrated any brain damage. At the New York Psychiatric Institute (Lewis, 1946) a neuropathological study of twelve *Macacus rhesus* monkeys subjected to electrically induced seizures under typical conditions failed to disclose any significant changes in the central nervous system detectable by standard techniques. However, it must be mentioned that Masserman (1946) in his fascinating work on the production of experimental neuroses in cats has found definitely impaired capacity for complex adaptations after shock treatment. It is possible that with more highly specialized and sensitive psychometric tests, subtle impairment of higher perceptive and integrative functions will be detectable similar to those resulting from known organic lesions of the brain.

The only common denominator in the action of all these types of shock therapy appears to be the production in the patient of an unconscious state. It may be that vital autonomic changes occur during the coma which accompanies and succeeds the convulsion; or you may be convinced, if you are psychologically minded, that the patient is frightened into a fight for existence and returns to reality in the process of saving his life; or if you are psychoanalytically minded, that there is an assault on pathological elements in the ego or a rebirth phenomenon from an intrauterine regression; or from the purely psychotherapeutic approach there is a release of inner tension and the formation of a new set or pattern of transformations occurring in the resolving of the period of amnesia. However, whatever may be the mode of action, we are, I think, justified in utilizing these forms of therapy for carefully selected patients until more scientific data are available that will permit us to make sound and unprejudiced predictions as to its final place in clinical psychiatry.

Psychosurgery.

We appear at the present time to be passing through a cranioclastic period in the evolution of clinical psychiatry, and time will permit of my making only some brief observations in regard to these developments. Various theories

have been postulated as to the manner in which the frontal lobes may be concerned in personality disorders and as to the application of various modifications of psychosurgery in their amelioration. While there is no doubt weighty clinical evidence to indicate the importance of the hypothalamus in the emotional aspects of behaviour, expressing itself through its sympathetic, parasympathetic or cortical connexions, we must not conclude that this is emotion itself; an emotion is a highly integrated, affective, autonomic and somatic reaction, in which the whole organism functions as a psycho-biological unit.

In the various forms of psychosurgery the aim appears to be the division of certain association fibres, in the anterior thalamic radiation, in the uncinate fasciculus connecting the orbital gyrus with the temporal lobe, or in the immediate subcortical neurons themselves.

Prefrontal Lobectomy.

Prefrontal lobectomy was introduced in the neurosurgical clinic at Minnesota in 1940, in preference to prefrontal leucotomy, as being a more accurate and scientific procedure in regard both to surgical technique itself and to more accurate localization of planes of section and areas of cerebral tissue involved. The results with this method, compared with those obtained with prefrontal leucotomy in the schizophrenic groups, exhibit little if any appreciable variation one way or the other.

A further application of this form of psychosurgery has been for the relief of pain of organic disease; it is particularly applicable where the affective or emotional component of the painful disorder is equally important with the local condition, or appears to be more disabling than the pain itself. Apparently psychosurgery alters the patient's reaction to pain without materially altering his or her ability to feel pain; it apparently divorces the fear, anticipation, anxiety, ideas of disaster or dependence in consequence of the disability it causes, from the actual pain itself, and so assists the patient to suffer the disability with fortitude or equanimity.

Transorbital Leucotomy.

While in Washington, District of Columbia, I was afforded the opportunity and privilege of seeing Walter Freeman, who with J. W. Watts introduced the original technique of Egas Moniz into the United States of America (Freeman, 1948), operating by his method of transorbital leucotomy. This method was originally introduced by Fianberti in Italy in 1937, but owing to the war his work was little known. The method has been utilized by Freeman fairly extensively since the end of the war; he had used it in over 150 cases at the time of my visit. In only two or three of these were any serious complications met; these were cases of hemiparesis due to accidental hæmorrhage, which eventually cleared up. I understand that he has had only one fatality in his total series of cases. In place of general anæsthesia Freeman uses electroconvulsive shock. Two shocks are given within two or three minutes of one another. The transorbital leucotome is introduced under the upper eyelid into the conjunctival sac in the mid-pupillary line and parallel with the bony ridge of the nose, and the orbital plate is easily perforated by a light tap of a suitable type hammer. The direction upwards of the leucotome at the correct angle is ensured by permitting it to lie fairly strongly on the eyeball. The leucotome itself consists of a circular shaft about four millimetres in diameter and about 12 centimetres long, tapering to a point about as sharp as a large-sized steel knitting needle. The shaft is graduated in centimetres, a double line being placed at the seven centimetres mark. When the leucotome has been inserted to the four centimetres level it is moved laterally to sever fibres in the lower portion of the frontothalamic radiation, and after being returned to the mid-position is again driven in to the seven centimetres mark, where lateral and medial rotations are made of about 15° to 20°; the leucotome is then withdrawn and moderate pressure applied over the orbital cavities for a few minutes to prevent as far as possible any excessive bleeding into the orbit. Should this occur the hæmatoma is usually resolved within a week or two. It may be necessary to administer one or two additional shocks to complete operation on the opposite frontal lobe, this being dependent on the skill of the operator or the reaction of the patient to the convulsive therapy, or on a combination of both factors.

Transorbital or supraorbital leucotomy undercuts areas 9 and 10 on the Brodmann chart, the removal of which by direct excision (topectomy) has likewise given most striking results, 10 out of 11 carefully selected patients being usefully occupied after discharge from hospital.

The simplicity of this modification of leucotomy, the approach to the cerebral tissues through an aseptic field with consequent elimination of a great many of the post-operative nursing hazards often encountered in the classical methods, the rapidity of recovery and the reduction of undesirable changes in the personality of the patients greatly impressed me. This procedure may run counter to sound surgical principles in some respects, but its apparent safety and rapidity in execution are noteworthy. I carefully examined the type of leucotome utilized in this procedure and am satisfied that the risk of serious hæmorrhage is quite remote; any traumatic hæmorrhage due to the leucotome itself would most likely arise from division of penetrating cortical vessels in the cerebrum itself rather than meningeal or surface vessels. Supra-orbital leucotomy in Freeman's hands has produced some excellent clinical results, and I think that his success can be traced largely to a very careful, painstaking selection of cases.

Cerebral Topectomy.

Cerebral topectomy is a modification of the gyrectomy practised by Penfield and introduced by Heath and Poole (1948). It has been taken up by a group of collaborators at the Columbia Presbyterian Medical Centre in New York, known as the Columbia Greystone Associates. It consists of the excision under an open bone-flap operation of certain areas of the cortex known chiefly as Brodmann's areas 9, 10 and 46. The removal of these special areas was found to be practically specific in the reduction of psychotic anxiety and other symptoms, without any impairment of intelligence, memory or other psychological functions and with remission of the psychosis and greatly improved overall mental outlook for the patient. In one particular case removal of Broca's area did not result in any aphasic symptoms. Such results fully support, if necessary, the contention that localization of functions to specific cortical areas is no longer tenable and only serve to emphasize the importance of the associative and compensatory functions of the so-called silent areas of the cerebrum as a whole. Nolan D. C. Lewis, who is the director of the New York State Psychiatric Institute, informed me that the results of these studies have been so interesting that they have led to the establishment of a new brain research project as a collaborative venture between the Columbia Presbyterian Medical Centre and the New York State Division of Mental Hygiene. This latter project will also no doubt explore the undercutting technique introduced by Scoville (1948), whereby the subcortical axons are divided and the cortex is left intact, a procedure claimed to be very promising.

Topectomy is obviously a more restricted operation on the frontal lobes, and the changes in personality following topectomy are claimed to be much less severe than those following leucotomy.

Cerebral Thalamectomy.

On the basis both of experiments carried out on decorticate animals and of those in which the hypothalamus has been directly stimulated, the conclusion has been reached that the hypothalamic region represents the neurophysiological concomitants of emotion and that the latter may be characterized by sympathetic and parasympathetic discharges from the hypothalamus; consequently Spiegel and Wycis of Philadelphia made a direct attack on the medial nucleus of the thalamus with a stereotaxic instrument based upon the Horsley-Clarke apparatus (Spiegel *et alii*, 1947). This latter is a mechanical device attached to certain anatomical landmarks on the skull in such a way

as to direct the electrocautery accurately to the medial thalamic nucleus. After the electrocoagulation the patients are said to develop incontinence, disorientation, masked expression, plateau speech and abolition of the emotional component of the psychosis; and clinical improvement is comparable with that observed after classical leucotomy. This conforms with the theory advanced by Freeman and Watts (1947) that the affective change in the patient is due to the retrograde atrophy of the thalamic centres after their connexions with the cortex have been severed.

Discussion.

The preliminary investigation of patients for psychosurgery varies considerably in different centres. At the Veterans Administration Hospital in Topeka, Kansas, leucotomies have been carried out strictly as a research project, and under such conditions scientific conclusions can be drawn bereft of personal prejudices. The value of such projects in a highly organized psychiatric centre cannot be over-emphasized. Here each patient is first studied very intensively, air encephalograms are prepared as a routine both before and after operation, and psychological test batteries are utilized before and after operation and even during the operation. Of the schizophrenic patients selected for special studies, most had been assaultive or depressed with marked intrapsychic tension and any patients having a lack of or flattening of affect had been excluded. With the specially selected patients encephalography is carried out before operation, as well as twenty-four and seventy-two hours after operation, and thenceforth once a month. In many of the neurosurgical clinics such measures are not performed as a routine, but air encephalograms are quite valuable when tumour or cerebral atrophy is suspected or to delimit the actual extent of the lateral ventricles. Sometimes special preparations are injected for purposes of post-operative X-ray examination to demonstrate the lines of incision.

Time does not permit me to deal with details of post-leucotomy observation and care, which are interesting, informative and most important to the neurosurgeon who undertakes the responsibilities of such an operation. However, I hope to make such information available for reference in another place and at an early date. Nor does time permit me to make anything like an adequate comparison or evaluation of the various methods, apart from the fact that my acquaintance with the subject is so limited. However, I might say that there is no doubt as to the important place leucotomy must take in our therapeutic armamentarium. Its greatest value appears to be in relieving emotional tension and distress, which are preeminently the main criteria, and the manifestations of morbid behaviour that flow from them.

The responsibility for advising such operations is a grave one and in my opinion should be taken only by psychiatrists, preferably in consultation, who from experience are competent to assess who should or who should not undergo leucotomy. Let us heed the necessary indications for such responsible decisions, lest we start an epidemic of hasty human experimentation, set going an avalanche of unwarranted expectations and finally experience our own ultimate embarrassment. As a warning to the enthusiasts, let me say that there are many leading psychiatric centres in England, America and the Continent that adopt a most conservative attitude towards such procedures, even to the extent of dismay or open condemnation. My experiences abroad lead me to the conclusion that the whole matter of leucotomy is still *sub judice*, and it is hoped that the elaborate research projects being undertaken, particularly in the New York centres, will clarify for us many difficult and conflicting assessments in the field of psychosurgery.

In view of public relations existing in our Australian communities, which are not strictly comparable in many respects with those in other English-speaking communities, and in view of learned counsels' recent opinions as to our legal status and the requirements of the law in such matters, the decision of the mental hygiene authorities some time ago to refrain from embarking on such projects in this State has proved to be a wise one, even though it evoked criticisms from some ill-informed persons that we were unprogressive and failed to keep pace with advanced methods of treatment, or, in words applicable to this particular instance, "failed to rush in where angels fear to tread". In consequence of the added experience and knowledge gained by workers in this field, legislation will no doubt be enacted at an early date that will permit this form of therapy to be made available to patients in this State.

Acknowledgement.

My thanks are due to the Public Service Board of New South Wales for permission to publish this paper.

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Reviews.

A TEXT-BOOK OF GENITO-URINARY SURGERY.

THE appearance of a "Textbook of Genito-Urinary Surgery", edited by Winsbury White and written by thirty-nine British authors, is most welcome.[1] It is a large volume, quite incapable of detailed review in a short notice such as this, but almost uniformly it is, as it should be, authoritative and sound. The words "almost uniformly" are used advisedly, for the book does possess one fault, that is, that there is a tendency here and there for the contributor, not so much to make a dispassionate statement of facts or to describe generally accepted standard procedures, as to give his own views and to describe his own operative technique. This criticism does not apply quite so much to Millin (who even so does not mention *osteitis pubis*) or to Wilson Hey, whose contributions have been made on this specific basis. It does, however, apply, for instance, to Morson's chapter on suprapubic prostatectomy, in which the only surgical procedure he describes in detail is his own perfectly sound modification of the Harris operation. As an article in a periodical it would be entirely in order, but for a text-book it is not exactly what is required. The Harris operation, one feels, is probably employed much more often than Morson's modification of it, and, if one of the two operations was to be described in full detail, the Harris operation would have been a better choice. The same criticism applies, and in greater measure, to Kenneth Walker's contribution on transurethral resection, which is an unfortunate chapter and could easily have been written ten years ago. One cannot believe that the statements made therein are truly representative of modern British urological practice. Again, Macdonald's chapter on bladder newgrowths occupies a bare eighteen pages, in the course of which he devotes eight lines to total cystectomy, stating that the operation has a high mortality and that the patient's condition is rarely sufficiently good to warrant it. It does not seem likely that these sentiments can really be shared by the majority of British urologists. This section of the book is far too short, but after all, with thirty-nine contributing authors, some degree of imbalance would be hard to avoid.

[1] "Textbook of Genito-Urinary Surgery", edited by H. P. Winsbury-White, M.B., Ch.B., F.R.C.S. (Edinburgh), F.R.C.S. (England); 1948. Edinburgh: E. and S. Livingstone, Limited. 9½" × 6½", pp. 1064, with many illustrations, some of them coloured. Price: 90s.

By and large, however, the book is a fine production. The illustrations are adequate and excellent, while the subject matter as a whole is thoroughly sound and some of it is superb. It is one of the best text-books available, and it is a matter for great satisfaction that such a book has been produced by British urologists.

NOTES FOR FOOD INSPECTORS.

WE have previously reviewed favourably the first and second editions of "Food Inspection Notes: A Handbook for Students" by two English "practising public health officers". The fact that a third edition has been called for within less than three years[1] shows that this little book, which fits easily into one's pocket, has met a definite want and has proved useful. As the preface to the first edition states, it was designed to extract and epitomise the knowledge available in larger volumes on the inspection of foods as required for examination purposes by intending food inspectors, and also to enable the qualified and experienced official to be reminded in a speedy manner of some essential point of food inspection work. It undoubtedly achieves those ends.

The work begins with meat inspection, giving notes on the examination of the live animal, on slaughter houses and methods of slaughtering and dressing, and on the anatomy and diseases of food animals. Imported meat, game, fish and shell-fish are considered. Then comes a chapter on milk and milk products, followed by one on miscellaneous foods. Short accounts are given of food poisoning and how to take samples for analysis; the book closes with a bibliography.

The book is one that medical officers of health might place with advantage in the hands of their inspectors whose duties include the oversight of food. If the medical officer is only occasionally himself engaged in health work, he will find it a handy way of refreshing his memory. It must be remembered, of course, that it has been prepared especially for English readers. The respiration rate of healthy sheep is given as 12 to 30 per minute, but at a recent Royal Show prize sheep in wool on a cool day were seen with respirations well above 100. We are glad to see that a few slips noted in our review in the second edition have been corrected. In the present one gelatin, not glycerin, is extracted from bones. Adrenaline is obtained from the adrenal, not renal, glands. Does the house fly (*Musca domestica*) deposit eggs "in both fresh and decomposing meat and even sores"? Is "bursted" (page 100) a good past participle? But these are minor matters as far as the use of the book is concerned, which we have pleasure in recommending to the notice of food inspectors.

PSYCHOSOMATIC DIAGNOSIS AND TREATMENT.

IT is difficult for an older practitioner to take seriously a book such as the "Synopsis of Psychosomatic Diagnosis and Treatment", by Flanders Dunbar, with the assistance of seven other doctors and the members of the staff of Columbia Presbyterian Medical Center, New York City.[2] It is assumed apparently that physicians do not appreciate that there is any relationship between the physical signs and the mental state of their patients. This book is addressed to general practitioners, and it is suggested that it is to be a guide-book in newer methods of diagnosis and treatment. Psychosomatic medicine is defined according to Osler. The origin and definition of the term psychosomatic are described, with the aid of very long words, and a psychodynamic summary is given on page 26. Introductory embryology and chronology are then summarized in a very learned manner, which leaves us somewhat dazed. L. W. Sontag, M.D., deals with determinants of predisposition to psychosomatic dysfunction and disease, the problem of proneness to psychosomatic disorder. The relationship of emotion to the nervous and locomotor systems and the gastro-intestinal system are described at some length. Bulimia is discussed on page 91, the author giving a description entirely opposed to that of Xenophon, which appears in the "March of the Ten Thousand". Xenophon states that bulimia is a condition of exhaustion and cold in which a man is unable to eat, whereas Dunbar states that it is a state of excessive appetite. The chapter on peptic ulcer has many elements of truth, but the phraseology is so obscure that it is not easy to understand the significance of the author's descriptions. For instance he states that: "In woman the conflict related to giving and receiving often centers about pregnancy. Giving birth to a child is obviously the most creative function of the female. The patient rejects pregnancy and the diarrhœa tends to serve as a substitute for the dreaded act of giving birth." There is a great deal more concerning the psyche and psychic trauma, and the impression may be gained at times that the outlook is more psychic than somatic. All the systems are dealt with, and it appears that many soldiers were said to have organic disease who had only a destructive personality profile. There is a great deal of information in this book, but it is rather scattered and buried under a phraseology which is not easy for the uninitiated to follow and is often laboured and discursive.

[1] "Food Inspection Notes: A Handbook for Students", by H. Hill, F.R.San.I., F.S.I.A., A.M.I.S.E., and F. Dodsworth, M.R.San.I., M.S.I.A.; Third Edition; 1949. London: H. K. Lewis and Company, Limited. 6½" × 4¼", pp. 140. Price: 7s. 6d.

[2] "Synopsis of Psychosomatic Diagnosis and Treatment", by Flanders Dunbar, M.D., with collaboration; 1948. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7½" × 4¾", pp. 506, with few illustrations. Price: 49s.

ELECTROCARDIOGRAPHIC TECHNIQUE.

A SLIM volume by Kurt Schnitzer presents with visual aids the finer points of how to take an electrocardiogram and how to hook up older electrocardiograph models for the newer techniques of unipolar and other type chest leads.[1]

Technicians and other electrocardiograph users would do well to read this book and to take heed of several points of commonly neglected technique. Too often do we see tracings which show only desultory efforts at eliminating A.C. interference, or more important still, no attempt at adjusting the base line to accommodate tall or deep complexes, with the result that the height of the *R* or *S* waves is indeterminable. Such measurements are of prime importance in unipolar electrocardiography.

Attention is drawn to the point that an electrocardiogram should not be taken less than two hours *post cibum*, or too soon after the smoking of a cigarette or the taking of a cold drink. The author mentions, but does not stress enough, the lack of value of an electrocardiogram taken on a digitalized patient.

Schnitzer reiterates an important point in the taking of chest leads, namely, the necessity for wiping off the paste from one position before proceeding to the next one to prevent surface conduction.

Illustrations are given of some common artefacts with hints for their elimination.

The book is useful for anyone buying an electrocardiographic machine and should be read by all technicians as a refresher.

SEX IN SOCIAL LIFE.

"SEX IN SOCIAL LIFE" (edited by Sybil Neville-Rolfe) is a book in which fifteen recognized authorities have collaborated to inform those of the general public, who may be interested, of the reasons and problems of sex behaviour.[2] There is a foreword by Sir Cyril Norwood (late headmaster of Harrow) in which he recommends the book "to all those who have to advise and control other human beings in the course of their work", and adds further, that "much may be gathered here to help understanding of self and sympathy with others, and to clear up the course of individual lives".

The book is divided into two parts. The first, "Sex and Science", surveys the scientific side of sex and deals with the biology of sex, the physiology of reproduction, psychology and sex, and sex and the family in primitive society. This section is well covered in simple language and is illustrated by thirty-eight drawings and diagrams.

The second part deals with the problems of "Sex and Society" and considers the contributing factors in maladjustment to sexual life. Failure in marriage is considered from both the personal and social aspects and it is suggested that not infrequently marriage may be quite unsatisfactory as regards sexual intercourse, unless the partners are well versed in the art of love. A chapter is devoted to

[1] "Electrocardiographic Technique: A Manual for Physicians, Nurses and Technicians", by Kurt Schnitzer, R.T., M.D.; 1949. New York: Grune and Stratton, Incorporated. 6" × 8½", pp. 100, with 46 illustrations. Price: $3.50.

[2] "Sex in Social Life", edited by Sybil Neville-Rolfe, O.B.E., with a foreword by Sir Cyril Norwood; 1949. London: George Allen and Unwin, Limited. 8½" × 5½", pp. 506, with illustrations. Price: 21s.

the consideration of this important subject, and most people would learn something of value from it.

The problems of the sex life of unmarried adults are considered and mention is made of some of the irregularities in sexual behaviour which may occur. It is realized that many women will never have the opportunity to marry and that many will seek satisfaction of their sexual needs without marriage.

Sex disturbance in middle life is dealt with, the male being considered as well as the female.

The book is well worth reading and can be especially recommended to all who seek a simple guide to the planning of comprehensive lectures on sex education.

THE EYES OF A CHILD.

"A CHILD'S EYES", by Professor Richard G. Scobee, is the title of a small book intended by the author to instruct parents, primarily, and doctors other than oculists, in the principles underlying the treatment of crossed eyes in children.[1] Why the learned professor of ophthalmology did not call his book "Crossed Eyes in Children" is just another of those problems so frequently set for us by our talented American colleagues. By not giving a clear indication of his subject matter, the author will fail to catch, in these hurried times, the swiftly crossing eye of many parents and physicians.

As to the people for whom he wishes to clarify the manifold problems of concomitant strabismus, this minor opus falls, as so many popularized presentations of unpopular subjects fall, between two stools. For the qualified medical practitioner, it is over-simplified, though it must be said that it would do a lot of doctors a lot of good to read the book. In these days, when many articles uphold the undoubted virtues of the general practitioner and belittle the efforts of those whose enthusiasm leads them to try to master some particular branch of medicine or surgery, it is refreshing to find someone telling the general physician to widen his horizon.

For the parents, unless in the 48 United States their average mental age is above the figure in slowly advancing Australia Fair, namely about thirteen and a half, the book is hopelessly intricate, with its diagrams of refracted rays and its employment of technical words, despite much effort at illustrative analogy.

For the ophthalmic surgeon, curiously, the book is not without interest, for it gives a colleague's point of view. The author advises early operation, which is in line with the direction of thought of many oculists today, but he skilfully evades the difficult decision of whether to operate before or after orthoptic treatment. He ridicules the idea that a squint follows an accident or illness, but the sequence is too common to dismiss with the phrase: *"Post hoc, ergo propter hoc."* He is missing the psychological factor.

To sum up, if Professor Scobee would consent to have his brain-child rent in twain, one-half for doctors and one for parents, he would do a great deal of good. But perhaps, like the parent confronted with Solomon's judgement, he would refuse.

MEDICAL EMERGENCIES.

FROM time to time every doctor is called to see a medical emergency, the treatment of which may not be entirely familiar to him, and in such a case the "Manual of Medical Emergencies" by S. C. Cullen and E. G. Gross will prove invaluable, and because of its handy size it can be readily carried in an attaché case or a motor-car pocket.[2] All the various cardiac emergencies are dealt with clearly and dogmatic lines of treatment are enumerated for them. Allergic conditions, diabetic and insulin coma, burns and sunstroke, to mention a few headings, are all completely discussed; however, as implied in the title, the book deals with medical emergencies only, and the sole surgical treatment mentioned is that of head injuries, which at times need surgical intervention when they progress beyond the scope of medical therapy.

The treatment of poisoning due to either drugs or commercial agents is well set out and this will enable the doctor to discover quickly and to use the correct antidote. In dealing with the treatment of acute mania, the doctor is wisely exhorted to remember that "there is no particular valor in being brave in these circumstances, and the physician should insist on plenty of help in subduing the patient". The only criticism of the book is from a local viewpoint in that as the book was published in the United States, it naturally contains details of the treatment for the bite of the black widow spider and the rattlesnake, while no mention is made of the bites of venomous Australian spiders and reptiles such as the funnel web spider or the tiger snake.

[1] "A Child's Eyes", by Richard G. Scobee, B.A., M.D., F.A.C.S.; 1949. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8½" × 5½", pp. 114, with 19 illustrations. Price: 15s.

[2] "Manual of Medical Emergencies", by Stuart C. Cullen, M.D., and E. G. Gross, M.D.; 1949. Chicago: The Year Book Publishers, Incorporated. 7" × 4¼", pp. 274, with 29 illustrations. Price: $3.75.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Notes to Lewis's Diet Charts." London: H. K. Lewis and Company, Limited. 8" × 5". Price: 1s.

These are notes on the rationale of the diet charts, which are intended as an aid to the general practitioner.

"The Surgical Clinics of North America" (issued every two months); 1949. Philadelphia and London: W. B. Saunders. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Mayo Clinic Number. 8" × 5", pp. 322, with illustrations. Price: £6 (paper binding) and £7 5s. (cloth binding) per clinic year.

This is a Mayo Clinic number. Six papers form a symposium on traumatic surgery; there are eighteen papers on other subjects.

"A Text-Book of Surgical Pathology", by Charles F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S. (Edinburgh), and Bruce M. Dick, M.B., F.R.C.S. (Edinburgh); Sixth Edition; 1949. London: J. and A. Churchill, Limited. 9" × 6", pp. 740, with 317 illustrations. Price: 45s.

Intended for senior students of surgery.

"A Synopsis of Obstetrics and Gynæcology", by Aleck W. Bourne, M.A., M.B., B.Ch. (Cambridge), F.R.C.S. (England), F.R.C.O.G.; Tenth Edition; 1949. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 7¾" × 4¾", pp. 536, with 167 illustrations. Price: 21s.

The author tries "to set before the student the basic core of facts which he must use while he gains increasing experience of obstetrics and gynæcology by contact with patients".

"Practical Anatomy: Revised and Rewritten", by W. E. Le Gros Clark, M.A., D.Sc., F.R.S., F.R.C.S.; Second Edition; 1949. London: Edward Arnold and Company. 8½" × 5½", pp. 516, with 268 illustrations, some of them coloured. Price: 30s.

Intended to be primarily a guide to the practical work undertaken by the student in the dissecting room.

"A Twentieth Century Physician: Being the Reminiscences of Sir Arthur Hurst, D.M., F.R.C.P."; with a foreword by Professor John A. Ryle, M.D., F.R.C.P.; 1949. London: Edward Arnold and Company. 8½" × 5½", pp. 214, with illustrations. Price: 15s.

Written by Hurst after his retirement and founded on his own recollections.

"Visual Development", by J. H. Prince, F.R.M.S., F.Z.S., F.B.O.A., F.S.M.C.; with a foreword by Professor H. Hartridge, M.A., M.D., Sc.D., M.R.C.P., F.R.S.; Volume I; 1949. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 434, with 190 illustrations, some of them coloured. Price: 50s.

Records the author's concept of certain aspects of vision after an expedition in many countries, collecting and examining animals.

"The Essentials of Chiropody", by Charles A. Pratt; Second Edition; 1949. London: H. K. Lewis and Company, Limited. 7¼" × 4½", pp. 172, with 34 illustrations, some coloured. Price: 10s. 6d.

Intended for the beginner in the study of chiropody.

The Medical Journal of Australia

SATURDAY, DECEMBER 17, 1949.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

RHEUMATIC FEVER.

If we wish to define a disease, we must be prepared to make clear its origin and its limits—the word define is related to the Latin *finis*, an end. In regard to rheumatic fever or acute rheumatism, it would be necessary to state that the disease was brought about by this or that agent or combination of agents and set of circumstances. Writing in Allbutt's "System of Medicine" at the dawn of this century, W. S. Church stated that rheumatic fever was more easily described than defined. That statement is still true. A great deal of investigation—clinical, pathological and biochemical—has been carried out during the last forty or fifty years. Many facts have been learned, but these are something like the coloured pieces of a mosaic—they have to be fitted into the general pattern, so that they lie in correct relationship with other pieces, touching certain facets, separated from others, and so that they have no undue prominence in the final picture. Those who try to keep abreast of the literature on rheumatism will recall the valuable reviews that have come from time to time from the committee of the American Rheumatism Association under the chairmanship of Philip Hench. Much of the work of recent years traverses the ground that was covered by workers at the end of the last century. This was made clear to readers of this journal in 1940 by H. Boyd Graham in a paper on rheumatic heart disease which he read at a meeting of the Victorian Branch of the British Medical Association. Rheumatism is to be the central theme of the congress to be held at Brisbane next May and June. Graham made his contribution memorable by quoting extracts from W. B. Cheadle's Harveian Lectures published in *The Lancet* in 1889. He referred to the "eternal freshness" of Cheadle's description, pointed out that it had stood the test of time and added that medicine today was still following the path which Cheadle blazed. Those who set out to discuss rheumatism at the Brisbane congress would be well advised to study Graham's paper; it will help them in their perspective. For the same reason we wish to draw attention to a recent review of the theories and evidence of the ætiology of rheumatic fever by B. H. Waksman.[1]

Waksman writes from the College of Physicians and Surgeons, of New York City; his article covers some 26 pages and he has a detailed list of 707 references to the literature. He starts off with the somewhat gloomy statement that rheumatic fever can at present only be classified as a member of a little understood group of diseases which includes rheumatoid arthritis, glomerulonephritis, *lupus erythematosus*, *periarteritis nodosa*, *thromboangiitis obliterans*, dermatomyositis, scleroderma and "perhaps others". At the end of his discussion, when all the pieces of mosaic have been laid out, face upwards, for inspection, the tendency is to try to force them into position, and it is necessary to keep constantly in mind the words "may be".

In the section of his work dealing with the factor of infection, Waksman points out that since Poynton and Paine carried out their investigations, the streptococci "have with few exceptions held the centre of the stage". Though certain workers (Cecil and others) obtained cultures of streptococci in more than half the cases which they studied, others did not always confirm these findings. Callow showed that cultures from patients who had rheumatic fever were not different from those taken from other patients who had respiratory diseases. This finding was confirmed. The previous workers (Cecil *et alii*) modified their statements and "it is now accepted, provisionally, that characteristic bacteria cannot be isolated from the blood stream, heart or joint tissues of rheumatic patients". Copeman reported in 1944 that rheumatic symptoms, fever and an increased sedimentation rate occurred in volunteers who had received injections of blood from a rheumatic patient. Waksman thinks that these observations ought to be confirmed. He states that the impetus to investigations since 1930 has been supplied by the studies of Coburn, who correlated the incidence of rheumatic fever with that of hæmolytic streptococcal infections and insisted that every attack of rheumatic fever must be preceded by such an infection, with an interval of two or three weeks. Coburn held that rheumatic fever was rare in the tropics, as were hæmolytic streptococcal infections, that it was commonest among poorer people, and that it had its greatest incidence in the winter and spring. Waksman shows how Coburn's contentions have had to be modified. Rheumatic fever is not uncommon in the tropics, but at the same time it is less frequent in warm than in cold climates. "The reason for the effect of climate remains in doubt." Much of the epidemiological investigation in rheumatic fever has been carried out with the implicit or explicit assumption that rheumatic fever is associated with upper respiratory streptococcal infections. It has been shown, however, that the throat flora of rheumatic patients differs in no way from that of other persons. At the same time Waksman points out that hæmolytic streptococci have been isolated from rheumatic patients before attacks by most workers in the field. He describes it as apparent that not all rheumatic attacks are preceded by a streptococcal infection. The fact that sulphonamide compounds and penicillin are ineffectual when administered after the onset of an attack, is additional proof that the initiating infection is not the direct "cause" of the disease, but acts

[1] *Medicine*, May, 1949.

only by starting in motion some more complex mechanism. Hench and his co-workers described the prodromal respiratory infections as "non-specific provocatives". Other types of infection may act as the initiator, and those described include malaria, dysentery and sandfly fever. Trauma, cold and fatigue may initiate attacks. Trauma plays a complex role, since it appears to some extent to determine the localization of the pathological changes which may appear.

Waksman points out that it is not known what process is set in motion by the various events. His general conclusion is that "it may be the adaptation syndrome of Selye, a non-specific allergic response, an increasing titer of auto-antibodies against some constituent of connective tissue or even the reactivation of a latent virus infection". His discussion on the factor of allergy, though somewhat lengthy, is full of interest. He points out that according to the suggestion of Zinsser and Yu in 1928 that streptococci might act as foci of infection in a hypersensitive host, rheumatic fever would be an allergic manifestation. As a result of extensive studies with different types of streptococci, Swift and his fellow workers suggested that rheumatic fever might represent infection in a hypersensitive host, while bacterial endocarditis represented infection with the same agent in an immune host—patients with bacterial endocarditis are insensitive to streptococci or their products, while rheumatic patients are sensitive. Waksman refers to the work of Birkhaug, who performed skin tests on rheumatic patients with a suspected allergic antigen. Others did similar work and a high percentage of reaction was obtained. The non-specificity of this kind of work has been emphasized. Waksman thinks that these and similar results may mean that rheumatic patients are sensitive to streptococci and their products only as a phase of a general allergic hyperirritability. In many ways the manifestations of rheumatic fever suggest an allergic process and the points favouring this view have been summarized—"absence of immunity, frequency of recurrence, sudden onset and relation to a precipitating illness". Waksman points out that objections have been raised to the view that rheumatic fever is a type of allergy. Harris and also Sayle have pointed out that the percentage of positive cutaneous reactions is less among rheumatic patients than in other streptococcal diseases and sometimes not significantly different from the percentage amongst normals; that many streptococcal diseases such as erysipelas are never followed by rheumatic diseases, although the organism is identical with other hæmolytic streptococci; that skin-positive patients need not have a rheumatic attack after a β streptococcal infection; and that the interval between the precipitating infection and the rheumatic exacerbation is almost constant, instead of decreasing with successive attacks as in other allergies. Waksman adds that the hypothesis that rheumatic fever is a non-specific allergy would do away with some objections, but it is apparent to him that something more is required for an adequate understanding of the disease. He refers to a new hypothesis which "has recently attracted considerable attention". According to this hypothesis (the reference is to W. J. Kerr), "rheumatic patients form antibodies against artificial antigens consisting of denatured proteins of their own tissues or of tissue proteins combined as haptens with some streptococcal or other material. The antibodies are capable of combining with the original undenatured or uncombined tissue protein, and clinical symptoms result whenever their titer is high enough to permit their combining with, and damaging, the tissues in question". Waksman mentions other scattered observations which are consistent with the hypothesis that formation of antibodies underlies rheumatic fever and its congeners.

The other factors discussed by Waksman are the factor of susceptibility, the factor of dietary deficiency, hyaluronidase and hyaluronic acid, and certain "other factors". It is concluded that susceptibility to rheumatic fever is an hereditary factor and that the frequency with which susceptible individuals contract rheumatic fever (this is known as the "penetrance") is influenced by internal factors such as sex, age, pregnancy, diabetes and thyreoid disease, and perhaps other factors undetermined as yet, and also by external factors such as climate and diet. If space permitted, it would be of interest to make more than passing reference to the production of "migrating polyarthritis" among experimental animals sensitized by a high salt intake and unilateral nephrectomy and given doses of adrenal cortical hormone or pituitary corticotrophin, or exposed to cold or some other damaging agent. In this regard one must recall the beneficial results lately reported in rheumatoid arthritis by the use of "Compound E". (See THE MEDICAL JOURNAL OF AUSTRALIA, October 1, 1949.)

Perhaps the most suitable note on which to end this short account of Waksman's review, though not the most optimistic, is that contained in his final sentence—that, except for post-mortem histological changes, no measurable change has been found in rheumatic fever to serve as a diagnostic tool and as a starting point for research.

Current Comment.

THE ACTION OF MERCURIAL DIURETICS IN CONGESTIVE CARDIAC FAILURE.

THE use of mercurial diuretics in congestive cardiac failure is now standard practice, and provided the renal function is satisfactory, other forms of œdema are now safely treated by these drugs without any of the fears once entertained by unadventurous therapists. The inclusion for injection in the British Pharmacopœia of mercurial preparations now emphasizes their everyday usage, and perhaps curiosity as to their action is somewhat languid. The official preparation contains sodium mersalylate in 10% aqueous solution with the addition of 5% theophylline. L. G. C. Pugh and V. L. Wyndham have set out to determine what are the circulatory effects of this combination, and have contrasted its action with that of the mercury salt alone.[1] It is generally agreed that the diuretic effect is due to a direct action of the mercurial salt on the kidney, by which the reabsorption of water and salt from the distal convoluted tubules is lessened, but the circulatory effects are less understood, especially as the position is complicated by the adjuvant action of another drug. Pugh and Wyndham carried out studies on eleven patients under treatment for various types of congestive heart failure. Most of them were seriously distressed by dyspnœa and œdema, and the venous pressure was greatly raised. It follows that exten-

[1] *Clinical Science*, Volume VIII, 1949, Numbers 1 and 2.

sive investigations were not always possible, but in every instance cardiac catheterization was performed, the pressure in the right auricle was estimated, and gas analyses of its contained blood were made. Oxygen consumption was measured directly or by spirometry, and the cardiac output estimated. A dye method for determining the blood volume was not found very satisfactory, and in some cases an attempt was made to estimate it during the experiment by observing the hæmoglobin content of the blood. Hourly measurement of the heart rate, blood pressure and urinary volume was made. In order to control the effect of the theophylline in the preparation, a special mercurial injection was prepared by the makers of the standard injection, and this was used without any addition of theophylline. The authors compared the findings with the results of venesection and found that the circulatory effects were similar, but of course there was a distinct difference in time, as venesection, or such a procedure as constricting the thighs by cuffs, acted much more quickly. In general it was found that the cardiac output rose, and the pressure in the right auricle fell. These effects began to be evident after two hours, and reached their peak in five to seven hours, declining and disappearing as the urinary output diminished once more. These findings applied to the use of mercurial diuretics with the addition of theophylline. When the pure mercurial alone was employed the rapid fall in intraauricular pressure was not seen, nor was the transient increase in the cardiac output, though a slow rise in output of the heart, accompanied by a fall in pressure in the right auricle, occurred later as diuresis was established. The quick response was apparently due to the theophylline. All details of the changes which occur after this form of treatment have not yet been worked out and the authors think that more work is needed before the mechanisms are clearly revealed. It would appear, however, that the immediate effect of mercurial diuretics on the circulation *per se* are slight, and those which can be detected later are due to the relief given by diuresis. The retention of the theophylline in the official preparation would seem to be justified, even if the effect is transient. One point mentioned by the authors is that they thought it advisable to reduce the dose of the mercurial when given alone, recognizing the toxic nature of the drug, for they point out that sudden death has occurred after the injection of a mercurial preparation, and it is possible that a sudden lowering of venous pressure may be an occasional vagary in its action on the circulatory system.

PERIODIC DISEASE.

RHYTHM is so inextricably associated with biological processes that we recognize it as part of life itself. It is natural that it should arouse interest in all human groups, whether in beliefs, superstitions, speculations or observations on the inner workings of living things, especially in relation to the external conditions of our known world. This interest inspires much of our scientific work, as on a lowlier level it may excuse the astrological column in newspapers. Therefore medical scientists and philosophers need no apology for wondering whether some of the intimate cellular and humoral aberrations which afflict our bodies may not be conditioned by inherent or derived fluctuations of a rhythmic or periodic type. A review of biological rhythms and cycles has recently been made by Nathaniel Kleitman, which covers a wide and fascinating field.[1] He points out that the terms rhythm, cycle and period are often used interchangeably, but brings some order into his summary by using the words according to defined meanings. Rhythm he takes to mean a regularly recurring quantitative change in some biological process in any living unit or group: it demands two conditions, that it should be of extrinsic origin and that it should persist for some time quite apart from external environment. Cycles, on the other hand, are intrinsic in origin, though potentially affected by internal or external conditions, and running a definite course. A good example is the cardiac cycle. Another extrinsic type of biological recurrence is periodicity, which is coupled to external variations, but is not necessarily regular. Thus diurnal periodicity may be quite regular, but that of meteorological origin may be irregular. This is, of course, sometimes hard to determine. Nature may devise variations on a theme, but the theme itself may be part of a larger and wider rhythmic pattern, like Elgar's well-known yet still mysterious "Enigma". Kleitman collects many instances of changes recurring after one or other of these patterns, arranging them in periods of less than twenty-four hours, diurnal periods, and periods of more than twenty-four hours, both related and unrelated to sex cycles. We may pass over the interesting cyclical education of the polycyclic human infant and the myriad examples of periodic diurnal activities of creatures ranging from the cockroach, mosquito and even more obnoxious insects to fishes, birds and mammals. With man social influences also have a bearing on his rhythms. As Kleitman remarks, even adaptation to night and day is a matter of acculturation rather than of acclimatization. It is the periods of wider range, varying from days to years, that excite the curiosity of physicians. Physical and mental variations have been observed experimentally, and data from vital statistics and meteorological and astronomical tables have also been used as a basis for deductions on biological changes. The question of the persistence of a rhythm becomes more difficult to understand here, and links up with some of those strange recurrent physical states which are often a clinical puzzle. H. A. Reimann has gathered together a number of pathological conditions which are observed to recur with strange regularity over a term of years without apparently causing permanent effects in other directions.[1] In these he includes periodic episodes of fever, abdominal pain, neutropenia, arthralgia, anaphylactoid purpura and paralysis. Even significant biochemical changes, which have been shown to accompany such episodic forms of illness, like the well-known alterations in the distribution of potassium in periodic paralysis, do not help us to understand the underlying causes. Periodic fever, of which Reimann gives sixteen examples, must be familiar to many clinicians, who have been quite unable to find a satisfactory explanation. One of the most interesting cases he reports is that of a woman who has been now observed and investigated for over thirty years and who, after innumerable investigations, still has attacks every week or fortnight. Without the drawing of inferences it should be recorded that she has had both her tonsils and her appendix removed. A number of cases of recurrent neutropenia have attracted attention in the literature also of recent times, but these are no more simple to explain than the instances of recurring benign peritonitis. The mechanism of the actual attacks is less obscure in anaphylactoid purpura and in angioneurotic œdema, but their cyclical occurrence still remains a mystery. Reiman discusses the possible causes of all these conditions, mentioning infection, allergy, endocrine disturbance and so forth, but these again refer to the manifestations themselves rather than to their intrinsic or extrinsic exciting cause. He comments on biological rhythm and remarks that the duration of the cycles has been found by some observers to correspond to seven days or a multiple thereof. This is certainly not always so, for the intervals between attacks of these kinds are often irregular and may vary widely in an individual; sometimes they are predictable and sometimes not. However, though it would seem rash to conclude that the selection of the seven-day week depends on some predetermined period in man or his environment, it is attractive as an hypothesis to regard recurrent episodes of disease as unusual manifestations of rhythm in human beings. As we hope that the ancient belief in an external malign cosmic influence is extinct, we may surely conclude that at least if the fault is not in the stars it may be buried deep in our biological make-up, but without blame to ourselves.

[1] *Physiological Reviews*, January, 1949.

[1] *The Journal of the American Medical Association*, September 17, 1949.

Abstracts from Medical Literature.

MEDICINE.

Dermatokinesthesis.

L. HALPERN (*The Journal of Nervous and Mental Disease*, January, 1949) states that when skin is raised in any part of the body and moved in one or the other direction, under normal conditions slight changes in direction are perceived. He calls this "dermatokinesthesia". Clinical observation shows that it has symptomatic significance, indicating deep sensibility. He claims that it is the only method to render possible segmental localization of some spinal syndromes.

The Coronary Blood Flow and the Electrocardiogram.

W. WÉGRIA *et alii* (*American Heart Journal*, July, 1949) have correlated the reduction of coronary blood flow and the appearance of electrocardiographic changes in anæsthetized dogs. They found that a reduction of blood flow of 10% to 35% did not as a rule produce any electrocardiographic changes. With a reduction of 35% to 70%, generally slight changes in the *RS-T* segment and in the *T* wave appeared. Occasionally no change was seen and sometimes the changes were pronounced. With a reduction of 70% to 100% in the blood flow the changes were always marked. When electrocardiographic changes were produced by the occlusion, minimal changes appeared within about a minute, increased progressively and reached their maximum within three to five minutes; they were reversible and disappeared within a few minutes of the release of the occlusion. It was demonstrated that a partial coronary occlusion might be sufficient to produce myocardial ischæmia, but too slight to produce electrocardiographic changes.

Ventricular Strain and Ventricular Hypertrophy.

DAVID LITTMAN (*The New England Journal of Medicine*, September 8, 1949) states that ventricular strain is a pathological state of imbalance that occurs with myocardial inability to contend with normal or abnormal stresses. It may cause reversible electrocardiographic alterations. Right ventricular strain is commonly seen with acutely or chronically elevated pulmonary pressures. Isolated strain of the left side of the heart occurs in coronary-artery inadequacy because of diminished ventricular ability to cope with normal stresses. Right ventricular strain is manifest graphically by *S-T* segment and *T* wave changes in the right ventricular precordial leads. When significant hypertrophy is added, the *R* waves in the same leads become abnormally tall and broad, whereas the *S* waves diminish in size. A graphic picture superficially resembling that found in left hypertrophy has been observed to develop from apparently normal records in patients with left ventricular disease recovering from congestive failure. It is seen in others who have no cardiac enlargement. The same pattern has also been seen to emerge in patients with rapidly increasing *angina pectoris* and to disappear with clinical improvement. Observations in these clinical states suggest that distinguishing differences can be noted between strain and hypertrophy of the left ventricle similar to those on the right side. The *S-T* segment and *T* wave abnormalities in precordial lead V5 or V6, or both, are considered to be manifestations of left ventricular strain. Enlargement of the *R* waves in the same leads constitutes evidence of left ventricular hypertrophy. These are usually seen together, but may occur separately.

Painless Myocardial Infarction.

M. E. LANDMAN *et alii* (*Archives of Internal Medicine*, June, 1949) found that out of 255 cases of myocardial infarction in which the diagnosis was verified by autopsy, no corresponding history or other evidence of symptoms of cardiac disease was present in 28. Furthermore, the authors received the impression, from a discrepancy between the age of the infarct observed at autopsy and the recorded time of onset of symptoms and signs, that in many cases attended by symptoms the actual infarction preceded the onset of the symptoms by an appreciable interval. It was also their impression that asymptomatic infarction of the heart should be suspected whenever an aged patient fails to respond after a surgical operation. Sudden cerebral insufficiency in aged persons or sudden failure in any case, with or without shock, is often explained by infarction of the heart.

Rheumatoid Spondylitis.

B. M. NORCROSS, H. M. ROBINS AND L. M. LOCKIE (*The Journal of the American Medical Association*, May 28, 1949) describe the use of *d*-tubocurarine in oil-wax suspension in rheumatoid spondylitis. They state that the pain and immobility of spondylitis can be relieved by X-ray treatment of the spine in 90% of cases. The authors also used 3% *d*-tubocurarine in 4·8% wax in peanut oil (175 units of standard curare per millilitre) injected intramuscularly every twenty-four to ninety-six hours, according to the response obtained in relaxing muscle spasm. Doses of 0·75 to 1·25 millilitres were given up to a total of 45 injections in each patient studied. The effects may last up to one hundred and twenty hours in some cases. Much relaxation of spasm with improvement in posture was noted in all cases and no habit-forming or toxic effects were observed.

Diabetes Mellitus.

ELLIOTT P. JOSLIN (*The Journal of the American Medical Association*, June 18, 1949) discusses modern treatment of *diabetes mellitus*. He discusses first the diagnosis and the use of a glucose tolerance test. He indicates that chronic mild diabetes is very prone to cause arteriosclerosis. He strongly advocates the use of insulin even in mild cases. He thinks treatment by a private or personal practitioner is better than treatment in out-patient clinics, because of the personal relationship. He awaits confirmation of the value of choline, one of the *B* complex vitamins, which has been advocated in doses of one to four grammes daily to prevent cirrhosis of the liver and arteriosclerosis in diabetes. Inositol has also been advocated for diabetes, but he prefers to obtain more facts. Vitamin *E* has been lauded, but he knows of no reason why he should use it. He describes the diabetes camps in the United States of America, especially those for children. He also mentions a new insulin, a modified protamine insulin which contains only 0·50 milligramme of protamine per 100 units of insulin, as compared with 1·25 milligrammes in protamine zinc insulin. It acts for twenty-eight to thirty hours, can be mixed with ordinary insulin, and is a boon to children as one dose often replaces the mixing of crystalline insulin and protamine zinc insulin. Further, the author advocates the use of nursing homes where patients can be taught to look after themselves.

Addiction Liability of Methadon.

HARRIS ISBELL AND VICTOR VOGEL (*The American Journal of Psychiatry*, June, 1949) state that, from the results of human experiments, there is no doubt that methadon is a dangerous addicting drug. Tolerance developed in both man and animals. Physical dependence is relatively mild, occurring after prolonged administration of large doses. In sufficient dose, euphoria of a long and sustained type is produced—a fact that must appeal to morphine addicts. It is pointed out that addiction is likely to spread rapidly when any drug is popular with morphine addicts. In ordinary legitimate medical use it is considered that methadon is equal in danger of addiction to morphine in the same circumstances—that is to say, slight. So long as the dose of either morphine or methadon is held to the minimum for the relief of pain, there is very little likelihood of addiction to either drug. The danger occurs when the doctor believes that the drug is not addicting and is careless in its use.

Studies on Headache.

C. KUNKLE, D. W. LUND AND P. J. MAHER (*Archives of Neurology and Psychiatry*, September, 1948) have studied certain aspects of the problem of headache by using a centrifuge in which a human being can be whirled. They show that headaches induced by compression of the scalp tissues were only slightly reduced by means of the centrifuge; the reason for this probably lay in distraction. However, headaches induced by histamine or the withdrawal of caffeine, which have a vascular origin, were eliminated during positive accelerations of two or three g. A similar response occurred with different types of clinical headache of vascular origin. The result of this work suggests one method of assessing the origin of headache.

Hypertensive and Ischæmic Heart Disease.

C. V. HARRISON AND P. WOOD (*British Heart Journal*, July, 1949) have made comparative clinical and pathological studies of 27 cases of hypertensive heart disease and 15 cases of ischæmic heart disease with 12 controls. The hypertensive cases were characterized clinically by even sex distribution, dyspnœa, steady deterioration, retinopathy, cerebral symptoms, impairment of renal function, anæmia, auricular fibrillation and clinical, radiographic and electrocardiographic evidence of left ventricular enlargement before the onset of heart failure; cardiac pain and infarction rarely occurred, and death was rarely abrupt. The ischæmic cases were characterized clinically by an

unequal sex distribution favouring men, the later age of women, infrequency of early dyspnœa, absence of anæmia, of retinopathy and of cerebral symptoms, good renal function, normal rhythm, normal heart size before failure and abrupt death. At autopsy the coronary arteries were injected and examined radiologically. It was found that moderate degrees of coronary atheroma do not necessarily cause narrowing; that the size of the coronary arteries varies directly with the heart weight in both normal and hypertrophied hearts, irrespective of the cause of the hypertrophy; that the coronary arteries are large with a smooth bore in the hypertensive cases and narrow and frequently occluded in the ischæmic; that in the hypertensive cases the heart weight varies with the degree of failure during life and not with the height of the blood pressure; that the coronary arterial size increases as the heart size increases, and that there is no evidence to indicate relative ischæmia of the ventricular muscle; and that in ischæmic cases cardiac hypertrophy is the rule and can be correlated with the duration of failure.

Myocardial Insufficiency.

G. R. HERMANN (*The Journal of the American Medical Association*, June 11, 1949) describes the use of a new mercurial diuretic in heart failure. He mentions a new preparation "Thiomerin", which he claims is less toxic and just as efficient as other diuretics. He also supports the other forms of treatment, such as salt restriction, fluid restriction and digitalis administration. "Thiomerin" is employed in the same doses and at the same intervals as other mercurial diuretics.

The Experimental Production of Arteriosclerosis.

A. STEINER *et alii* (*American Heart Journal*, July, 1949) have produced arteriosclerosis in dogs by feeding them with cholesterol and thiouracil. It was found necessary to maintain the serum cholesterol level above 450 milligrammes per 100 millilitres for more than a year before arteriosclerotic lesions became evident. The lesions had the same anatomical distribution and sites of predilection as lesions in man and they had the same morphological features.

Essential Hypertension.

J. E. WAKERLIN (*Annals of Internal Medicine*, August, 1949) discusses recent advances in the pathogenesis and treatment of essential hypertension. He states that essential hypertension is fundamentally due to slight generalized arteriolar vasoconstriction of the systemic circulation, with compensatory increased force of cardiac contraction. The fundamental pathogenesis of this vasoconstriction is not yet established; increased tone of the vasomotor system, a renal pressor effect, or an altered anterior pituitary-adrenal cortex relationship may be involved. Cortico-hypothalamic imbalance may exert an effect through any of these three mechanisms, and unquestionably this factor, through increased vasomotor tone, plays an aggravating role, even though the elevated blood pressure of essential hypertension may be primarily on a renal, endocrine or other basis. The treatment of essential hypertension is still relatively unsatisfactory. Medical management includes psychotherapy, judicious reordering of the patient's living, and the intermittent use of sedatives, particularly when the first two measures do not relieve nervous tension. The nitrites, nitrates and xanthine derivatives may be used, although their value is questioned. The use of sodium thiocyanate is on the wane, although with due allowance for its shortcomings, the drug may have some value. The possible anti-hypertensive effects of restriction of protein and sodium chloride are being redetermined. Certain sympathetic-blocking drugs are under study. Anti-hypertensive renal and marine oil principles are still in the animal stage of investigation. Of the many other medicinal agents recommended for essential hypertension, none has been shown to be of definite value. Sympathectomy may be curative for a minority of essential hypertensives and of possible value for others. Further and more intimate studies of the surgical treatment of essential hypertension are necessary. The solution of the enigma of essential hypertension is dependent upon further work in the laboratory and clinic, especially toward determination of causes, pathogenesis, and more exact patho-physiology. Once these are known, treatment will become rational, specific and more effective.

The Changing Site of Duodenal Ulcer.

I. AIRD (*Edinburgh Medical Journal*, March, 1949) states that twenty to thirty years ago the commonest site of a duodenal ulcer submitted to operation was the anterior wall of the first part of the duodenum: to explain the frequent occurrence of ulcer at this site Wilkie advanced the theory of a jet of acid juice directed by the pyloric canal against the mucous membrane in the locality. In the last few years, on the other hand, ulcer of the anterior duodenal wall has been rare in the author's experience and there has been a remarkably increased incidence of ulcer of the posterior wall.

Stomatitis and Dermatophytosis Occurring during Streptomycin Therapy.

J. C. MULHEARN (*Diseases of the Chest*, August, 1949) reports several cases of pharyngeal ulceration, also three cases of recrudescence of pre-existing dermatophytosis, in patients undergoing treatment with streptomycin. Ulceration of the vulva occurred along with the pharyngeal ulceration in one case. The author suggests that streptomycin may diminish bodily resistance to pre-existing fungous infection.

Massive Penicillin Therapy in Abdominal Actinomycosis.

G. E. SANDFORD AND R. O. BARNES (*Surgery*, May, 1949) state that abdominal actinomycosis causes half the fatalities of the disease, although this form makes up but one-fifth of the total number of cases. Until the introduction of the antibiotics the outlook was poor. Morton has classified cases of abdominal actinomycosis as follows: (*a*) those resembling acute appendicitis with a residual abscess or fistula—prognosis good; (*b*) those associated with a mass in the lower right quadrant and no obstruction—mortality rate about 40%; (*c*) those associated with rapid extension into retroperitoneal cellular planes with psoas spasm—this group has almost uniformly had a fatal termination. There seems to be some evidence that concomitant infection facilitates the spread of the fungus either by reducing the oxygen potential or by specific synergism. Adequate surgical treatment and supportive measures are essential, but antibiotics give the best means of reducing the mortality. Sulphonamides should be used in conjunction with penicillin, for some strains are sensitive to these drugs, which also assist in the control of the secondary infection. The sensitivity of the various strains to penicillin varies widely. In view of the granulation tissue surrounding the numerous foci, high blood levels are required to penetrate to the organism. Massive penicillin therapy has had dramatic effect. Doses range up to 500,000 units given intramuscularly every three hours and 10,000,000 units in one litre of normal saline given daily by the intravenous drip method. No toxic effects were noted.

Chronic Lymphatic Leuchæmia.

I. H. LAWRENCE *et alii* (*The Journal of the American Medical Association*, June 18, 1949) discuss the treatment of chronic lymphatic leuchæmia with radioactive phosphorus. In a series described 100 patients were treated with P^{32} and X-ray therapy. Dosage was worked out individually and according to the therapeutic response. The authors conclude that the results of treatment were better than those obtained previously by other methods.

Cerebral Aneurysm.

BERNARD J. ALPERS AND JAMES J. RYAN (*The Journal of Nervous and Mental Disease*, March, 1949) state that in their experience the diagnosis of aneurysm involving the cerebral arteries is still often based on relatively typical clinical findings. The diagnosis is made upon two factors: (i) the history of recurrent bouts of head pain, usually unilateral and often frontal or supraorbital in location, and (ii) the development of progressive or acute cranial nerve paralysis, associated often with head pain, and involving chiefly one or more of the oculomotor nuclei. The authors consider this syndrome so reliable that they have operated in two cases in which arteriograms did not reveal any abnormality of the cerebral vessels. The diagnosis of aneurysm was verified at operation.

Bronchoscopy in Asthma.

G. L. WALDBOTT (*The Journal of Thoracic Surgery*, August, 1949) states that the chief indication for bronchoscopic treatment in bronchial asthma is any threat of asphyxia which might rise from the patient's inability to expel thick tenacious mucus. In a moribund asthmatic patient, therefore, bronchoscopy is as obligatory a procedure as tracheotomy in a patient about to become asphyxiated in diphtheria or the removal of a foreign body from a bronchus. Another purpose of bronchoscopic treatment is the breaking up of a chronic state of asthma regardless of its severity. The treatment is contraindicated in asthma of short duration, in asthma associated with allergic shock and when there is no clinical evidence of mucous plugs in the bronchi.

British Medical Association News.

ANNUAL MEETING.

THE annual meeting of the South Australian Branch of the British Medical Association was held in the Verco Theatre of the Institute of Medical and Veterinary Science, Adelaide, on June 29, 1949, DR. A. D. LAMPHEE, the President, in the chair.

Annual Report of the Council.

The annual report of the Council was received and adopted on the motion of Dr. K. S. Hetzel, seconded by Dr. A. R. Southwood. The annual report is as follows.

At the annual general meeting of the Branch held on June 23, 1948, the following officers and members of the Council were elected:

President: Dr. A. D. Lamphee.
Vice-President: Dr. C. O. F. Rieger.
Honorary Treasurer: Dr. P. T. S. Cherry.
Honorary Medical Secretary: Dr. Robert F. West.
Ordinary Members of Council: Dr. R. L. Thorold Grant, Dr. B. S. Hanson, Dr. A. Britten Jones and Dr. H. Keith Pavy (country representative on the Council).

At a meeting of the Council held on July 1, 1948, the following subcommittees were appointed:

Scientific: Dr. J. Estcourt Hughes, Dr. A. Britten Jones and Dr. R. L. Thorold Grant.
Contract Practice and Medical Planning: Dr. R. John Verco, Dr. S. J. Douglas and Dr. L. L. Davey.
Ethics: Dr. B. S. Hanson and Dr. H. Keith Pavy.
Parliamentary Bills: Sir Henry Newland and Dr. R. John Verco.
Publicity: Dr. A. D. Lamphee, Dr. R. John Verco, Dr. F. L. Wall, Dr. S. J. Douglas (coopted February 25, 1949), Dr. L. C. E. Lindon, Dr. W. G. Norman, Dr. F. B. Turner (coopted April 7, 1949).
Library: Sir Henry Newland, Dr. R. L. Thorold Grant, Dr. J. Estcourt Hughes and Dr. R. F. West.
Salaries: Dr. S. J. Douglas and Dr. A. Britten Jones.
Tuberculosis: Dr. H. M. Jay, Dr. D. R. W. Cowan, Dr. J. L. Hayward, Dr. K. S. Hetzel and Dr. P. S. Messent.

The president is *ex officio* a member of all committees, as are also the immediate past president, vice-president, honorary treasurer and honorary medical secretary.

At a meeting of the Council, held on July 1, 1948, Dr. G. Wien Smith, of Clare, was appointed to serve on the Council as a country member until the date of the next annual meeting (*vide* Rule 44), thus completing the unfinished term of Dr. Bennett, who retired on December 4, 1947.

Monthly Scientific Meetings.

Eight meetings were held during the year up to May 12, 1949.

The following programme was carried out:

July 29, 1948: Film evening: "Method of Treatment of Fractures."

September 30, 1948: Dr. E. F. Gartrell: "Some Aspects of Subacute Bacterial Endocarditis."

October 12, 1948: Dr. F. A. Maguire: "The Use and Abuse of the Curette" (in combination with the South Australia Fellows of the Royal College of Obstetricians and Gynæcologists).

November 18, 1948: Dr. D'Arcy Sutherland: "Recent Developments in Surgical Treatment of Chest Diseases."

December 16, 1948: Dr. Noel Bonnin: "Recent Developments in Genito-Urinary Surgery."

March 31, 1949: Dr. W. John Close: "The Prostate: Some Commonly Disregarded Precepts and Principles."

May 12, 1949: Listerian Oration delivered by Dr. C. W. B. Littlejohn, of Melbourne: "Lister as the First Modern Traumatic Surgeon."

In addition to the above, members were invited by the State Committee of the Royal Australasian College of Surgeons to the lecture given by Dr. Julian Orm Smith on July 23, 1948, and by The Royal Australasian College of Physicians to the two lectures given by Professor Pickering on April 21 and 28, 1949.

The Post-Graduate Committee in Medicine also invited members to the lecture given by Dr. A. H. Penington on January 26, 1949, and the Australasian Association of Psychiatrists to meetings held on February 22 and May 3, 1949.

Membership.

The membership of the Branch is 572, an increase of 15 over the previous year. The number of new members elected was 28 and the balance results from deaths, transfers and resignations.

It is with sincere regret that the Council records the deaths of Dr. J. Harvey Johnston, Dr. R. W. Gibson, Dr. T. W. Tassie, Dr. J. Walter Browne and Dr. F. J. Jude.

Representation on Boards et cetera.

Medical Board of South Australia: Dr. E. Britten Jones.
Dental Board of South Australia: Dr. W. John Close.
Nurses' Board of South Australia: Dr. A. B. Russell.

Attendances at Council and Committee Meetings.	Council.	Contract Practice and Medical Planning.	Ethics.	Scientific.	Salaries.	Publicity.	Library.
CHERRY, P. T. S.	12	3	2	1	—	—	—
DAVEY, L. L.	14	5	—	—	—	—	—
DOUGLAS, S. J.	13	6	—	—	2	5	—
GRANT, R. L. THOROLD ..	14	—	—	2	1	—	2
HANSON, B. S.	13	—	1	—	—	—	—
HUGHES, J. ESTCOURT ..	13	—	—	2	—	—	2
JONES, A. BRITTEN	12	—	—	2	1	—	—
LAMPHEE, A. D.	14	6	2	2	2	4	—
MALLEN, L. R.[1]	4	—	—	—	—	—	—
NEWLAND, H. S.[2]	8	—	—	—	—	—	1
PAVY, H. KEITH	7	—	—	—	—	—	—
RIEGER, C. O. F.	12	7	2	2	2	—	—
SMITH, G. WIEN	7	—	—	—	—	—	—
VERCO, R. JOHN	13	5	—	—	—	5	—
WALL, F. L.	14	6	1	2	2	5	—
WEST, R. F.	12	2	2	1	—	—	2
Meetings held up to May 5, 1949	14	7	2	2	2	5	2

[1] Appointed February 3, 1949.

[2] Resigned January 10, 1949.

Australian Aerial Medical Services Council: Dr. J. M. Dwyer.
Australian Red Cross Medical Services Advisory Committee: Dr. F. L. Wall.
Federal Council of the British Medical Association in Australia: Dr. R. John Verco and Dr. L. R. Mallen.
Saint John Ambulance Association: Dr. H. H. Hurst.
Representative of "The Medical Journal of Australia": Dr. E. F. Gartrell.
British Medical Hall Company Directorate: Dr. G. H. Burnell and Dr. P. T. S. Cherry.
Mothers and Babies' Health Association: Dr. R. John Verco.
Panel of Medical Referees under the Provisions of Section 97(a), Subsection 7, of the Workmen's Compensation Act: Sir Trent de Crespigny, Dr. K. S. Hetzel, Dr. F. Ray Hone, Dr. E. Britten Jones, Dr. G. A. Lendon, Dr. E. McLaughlin.
Bankers' Health Society: Dr. J. Estcourt Hughes.
Certifying Medical Practitioner under Part IX of the Workmen's Compensation Act: Dr. C. H. Schafer.
Representative on Central Council of the Association: Dr. J. H. Anderson.

Resignation of Sir Henry Newland as a Representative of the Council of the South Australian Branch on the Federal Council of the British Medical Association in Australia.

On January 10, 1949, Sir Henry Newland tendered his resignation as a representative of the Council of the Branch on the Federal Council of the British Medical Association in Australia. At a meeting of the Council of the Branch, held on January 13, 1949, the resignation was accepted with regret when it was decided to place on record the valuable services rendered to the profession by Sir Henry over a long period of years. Sir Henry was first appointed as representative of the Branch to the Federal Council on November 12, 1920 (in place of Dr. F. S. Hone), since when he has served continuously on the Federal Council, and occupied the position for the last twenty-one years. Sir Henry has been closely associated with Branch affairs for over forty-eight years and has been a member of the Branch Council for approximately twenty-nine years, and it is a matter of regret that the services of so valuable a member have been lost to the Branch Council. In view of recent medico-political events his loss will be felt very keenly, not only by the members of this Branch, but by the whole of the profession throughout Australia.

At its meeting in Melbourne on March 1 to 4, 1949, the Federal Council adopted the following minute of appreciation.

> The Federal Council of the British Medical Association in Australia at its meeting in Melbourne on March 1, 1949, wishes to place on record, on the occasion of his retirement as President, its appreciation and gratitude to Sir Henry Simpson Newland for his unceasing labours during many years of service. Coming to the Federal Committee as a representative of the South Australian Branch in 1921, Sir Henry Newland at once took a prominent part in its deliberations and in 1930 was elected President. When in 1933 the Federal Committee became the Federal Council, Sir Henry continued in the office of President and has served with distinction since that time. During the difficult years of war his interest did not cease nor his energy falter. As a leader he has set a high standard and the Council knows that this influence will extend far into the future. He has the affectionate regard of every member.

At a meeting of the Branch Council, held on February 3, 1949, Dr. L. R. Mallen, of Riverton, was appointed in place of Sir Henry to represent the Branch (together with Dr. R. John Verco) on the Federal Council of the British Medical Association in Australia.

Model Common Form of Agreement.

During the year a new lodge agreement was concluded between representatives of the Council and the United Friendly Societies Council of South Australia and became operative in this State as from the quarter commencing December 1, 1948. The agreement is working smoothly and it should be noted that the agreement is for one year only and that provision is made for altering the capitation fee in accordance with the rise and fall in the State basic wage. This is thought to be the most equitable method of calculating the unit rate. In view of the fact that negotiations were finalized with the friendly societies in March, 1948, and that the agreement did not commence in this State until December, 1948, the friendly societies advised that they were willing to consider an increase in the capitation rate (in accordance with the rise in the State basic wage) in March, 1949, instead of waiting until December, 1949.

A further conference will shortly be held between representatives of the Contract Practice Subcommittee and representatives of the Friendly Societies Council to decide on the new capitation rate, in view of the fact that the State basic wage is now £6 5s. in lieu of £5 6s. which it was at the beginning of the new agreement. The new rate will apply for a period of one year (*vide* Clause 13).

Sections.

Section of Anæsthetics.—The annual report of the section for the year 1947-1948 is as follows:

At the annual general meeting held on September 30, 1947, the following officers were elected:

Chairman: Dr. S. R. Hecker.
Vice-President: Dr. Mary Burnell.
Australian Society of Anæsthetists Representative: Dr. Gilbert Brown.
Secretary-Treasurer: Dr. J. E. Barker.

During the year the following meetings were held:
February 5: Main topic, "Curare", introduced by Dr. M. Burnell.
April 15: Film evening. Series of films on anæsthesia and allied subjects.
July 7: Main topic, "Endotracheal Anæsthesia", introduced by Dr. S. R. Hecker.

Thirteen members attended on February 5 and eleven on July 7.

During the year food parcels were packed and sent to anæsthetists in Great Britain.

In August, 1948, the annual meeting of the Australian Association of Anæsthetists was held in Perth in conjunction with the Australasian Medical Congress, and seven members from this State attended.

Eye, Ear, Nose and Throat Section.—The annual report of this section for the year ended March 2, 1949, states:

During the year seven meetings were held, three of them especially to discuss lodge agreements. The average attendance was nine members, and there are seventeen members of this section. Meetings were held as follows:

March 16, 1948: Annual meeting.
March 30, 1948: Lodge agreements.
May 4, 1948: Clinical evening and lodge agreements.
June 22, 1948: Clinical evening.
July 14, 1948: Lodge agreements.
October 5, 1948: Clinical evening and lodge agreements.
January 18, 1949: Lodge agreements.

The office-bearers are:
Chairman: Dr. F. J. B. Miller.
Vice-Chairman: Dr. R. H. von der Borch.
Secretary and Treasurer: Dr. E. Couper Black.
Committeeman: Dr. H. M. Jay.

Section of Clinical Medicine.—The first meeting of the section since the cessation of hostilities in World War II was held on February 17, 1949. The annual general meeting of this section, combined with a clinical meeting, took place on May 17, 1949, when the following office-bearers were elected:

Chairman: Dr. M. E. Chinner.
Honorary Secretary and Treasurer: Dr. C. B. Sangster.
Committeemen: Dr. Mark Bonnin, Dr. Ivan Magarey and Dr. Hugh Gilmore.

Membership.—Forty-one members of the British Medical Association are financial members of the section. Members of the British Medical Association are urged to join the section, the activities of which may be regarded as an integral part of post-graduate education. It is intended to hold meetings every two or three months throughout the year.

Finances.—There is a balance of £22 5s. 1d. to the credit of the section with the Savings Bank of South Australia.

Northern Medical Association: Report for Year ended June 30, 1949.—Four meetings were held during the year. The first at Riverton. Dr. Guy Lendon and Dr. A. Britten Jones gave addresses on the medical and surgical aspects of the dyspepsias. The second at Terowie. Dr. Mallen showed films lent by Wyeth Brothers Incorporated. The third at Clare. This meeting took the form of a refresher course arranged by the Post-Graduate Committee. Programme: Dr. Ivan Magarey, "Investigations of Pyrexia in Infancy"; Dr. K. S. Hetzel, "Fits and Faints"; Dr. A. C. McEachern, "Recent Advances in Post-Operative Cases"; Dr. W. F. Joynt, "Management of Anti-Partum Hæmorrhage". The fourth at Port Pirie. Professor Pickering (Sims Travelling Professor

for 1949) on "Hypertension". There are twenty-one financial members of the association, and the average attendance at meetings was fourteen. The office-bearers are: *Chairman*, Dr. L. R. Mallen; *Honorary Secretary*, Dr. G. Wien Smith.

Schedule of Fees Under Workmen's Compensation Act.

With a view to securing an increase in the scale of fees payable for medical treatment of injured workmen under the *Workmen's Compensation Act*, a conference between the Contract Practice Committee and a subcommittee of the Fire and Accident Underwriters Association of South Australia was held on March 14, 1949. At that meeting the Contract Practice Subcommittee submitted a proposed new schedule of fees (drafted after several previous meetings of the committee) to the underwriters for discussion. The new schedule has been adopted from a similar scale on which negotiations are taking place between the Victorian Branch and the underwriters in that State at the present time and provides for a substantial increase in the existing fees. The underwriters agreed that some increase was necessary and were in sympathy with the request of the committee for a revision of the fees. The meeting decided to leave the matter in abeyance for a short time, pending an agreement being arrived at in Victoria. A further conference with the underwriters is to be held shortly.

National Health Service.

The latest policy of the Federal Council with regard to the form of control, and also the conditions which should obtain in a fee-for-service scheme of government medical benefits, is defined in the following resolutions adopted by the Council at its two recent meetings.

It is considered by the Federal Council that the essential points of any national health services are:

1. That payment be on the refund system exclusively.
2. That there should be a scale of benefits and not a scale of fees.
3. That there be no experimental health centres as envisaged by the Minister for Health under the *National Health Service Act*, 1948.

The policy of the Federal Council is defined by means of the following resolutions passed at a meeting held in Sydney on December 11, 1948:

(*a*) That the right of any member of the public to obtain medical benefits in respect of a medical service received, shall not be dependent on the existence of any arrangement, agreement, or contract between the doctor providing the service and the Government.

(*b*) That the willingness of any doctor to cooperate in the machinery for enabling some of his patients to obtain medical benefits shall not debar him from entering into private arrangements with patients to the exclusion of the government scheme, provided such arrangements are acceptable to both parties.

(*c*) That the medical profession is unwilling to undertake the clerical work and liabilities involved in acting as "agent for the patient" in obtaining medical benefits, and insist that payment be by the refund system exclusively.

(*d*) That the medical profession refuses to make available to any third party, lay or medical, the clinical records of patients as part of the machinery for enabling patients to obtain medical benefits.

(*e*) That the medical profession refuses to admit the right of the Government to fix a fee of which it pays only a part, and demands that a scale of benefits, and not a scale of fees, be laid down.

The Federal Council advises all members not to cooperate in any fee-for-service scheme of government medical benefits which is contrary to the policy of the Federal Council, and to refrain from replying or responding to any approach by the Government to them as individuals, without obtaining the consent of the Branch Council. Members are advised that the Federal Council will oppose any attempt by the Government to implement by coercion of medical practitioners any form of medical service which is contrary to the policy of the Federal Council.

As members are aware, with a view to maintaining the freedom of the medical profession and rendering material assistance to any member who may suffer as a result of loyally abiding by the policy laid down by the Federal Council, a Federal Independence Fund was launched throughout all the States in March last.

Contributions received from members of this Branch amount to just over £4250 at the present time, and although this is quite a good response, it is felt that there are many members who may have omitted to subscribe to the fund so far. It is emphasized once again that any unexpended portion of the fund will be refunded to subscribers on a *pro rata* basis according to the amount subscribed.

Two special general meetings of members were held throughout the year, both of which were well attended. At the special meeting held on March 24, 1949, the following resolution was carried unanimously:

> This Special General Meeting of members of the South Australian Branch of the British Medical Association desires to express its confidence, appreciation and support of the action taken by the Federal Council of the British Medical Association in Australia to protect the interests of the medical profession and the people of Australia.

THE MEDICAL JOURNAL OF AUSTRALIA of February 5, 1949, contains a complete and connected story of the negotiations between the Commonwealth Government and the Federal Council from 1944 up to the present time.

Pharmaceutical Benefits (Amendment) Act, 1949.

As members are aware, the act has now been amended to read as follows:

7A. Except as prescribed a medical practitioner shall not write a prescription for a supply to a person entitled to pharmaceutical benefits,

(*a*) of an uncompounded medicine the name of which or a medicinal compound the formula of which is contained or is deemed to be included in the Commonwealth Pharmaceutical Formulary; or

(*b*) of a material or appliance the name of which is contained in the prescribed addendum to the Commonwealth Pharmaceutical Formulary,

otherwise than on a prescription form supplied by the Commonwealth for the purposes of this act. Penalty, £50. The section is to come into operation on a date to be fixed by proclamation.

At a meeting of the Federal Council held on March 1 to 4, 1949, the Council resolved:

> That the Federal Council is completely opposed to the regulations to the *Pharmaceutical Benefits Act* which makes it an offence for a doctor to prescribe any medicines contained in the Government Formulary other than on a government form. The Federal Council is determined to test the legality of these regulations and, in the meantime, will stand behind any member who may be prosecuted under them.
>
> That the President be authorized to take whatever steps are necessary to test the legality of the proposed regulations under the *Pharmaceutical Benefits Act*.

In reference to copies of the formulary and forms which it is expected that members will shortly begin to receive, members were advised on April 6, 1949, that as the association's legal advisers have intimated their opinion that the *Pharmaceutical Benefits Act* is invalid, the validity of which will be tested at the appropriate time, they should formally receive and preserve any documents relating to the act which might be forwarded to them by the Commonwealth Government.

Publicity.

At a special general meeting of members of the Branch, held on March 24, 1949, the need for an adequate Press publicity campaign was stressed. It was felt by the majority of members present that many members of the general public were unaware of the real reasons for the opposition of the profession to the *Pharmaceutical* and *National Health Service Acts*, and that in order to retain the sympathy of the public, some plan of general public education should be proceeded with.

At a meeting of the Council held on April 7, 1949, it was decided to make an immediate appeal to members for funds to assist in the conduct of a local publicity campaign, and at the present time an amount of approximately £250 has been subscribed.

The Council has engaged the services of a firm of professional publicists and has in addition coopted on the local publicity committee three non-members of the Branch Council. So far seven paid advertisements have been inserted in the columns of *The Advertiser*, which have appeared on successive Saturdays, and it is believed that these advertisements have been favourably received. Other avenues of publicity have been thoroughly explored by the committee and publicity material is being distributed to the public in other ways. It is emphasized, however, that the cost of achieving suitable publicity necessitates the spending of

considerable sums of money from time to time, and the Council appeals to members who have not yet subscribed to the Publicity Fund to do so immediately in order that the objects of the campaign may be fulfilled.

Hospital Policy.

Members are advised that at its meeting held on March 1 the Federal Council resolved:

(*a*) That the Federal Council is of the opinion that public hospitals should be open to and provide accommodation for all classes of patients—public bed, intermediate and private, according to their means—and that intermediate and private patients should pay for medical attention. That all reputable medical practitioners should be entitled to render services to intermediate and private patients in all public hospitals, and that Branch Councils be asked to implement this policy.

(*b*) That the Federal Council is of the opinion that where public hospitals are available free to all members of the community and the whole financial responsibility for their upkeep has been accepted by the Government, no reason exists for the continuation of the honorary service.

(*c*) That in view of the fact that the honorary system confers freedom from government control, the Federal Council is of the opinion that it is inopportune at the present time to initiate steps for its abolition.

Informal Talks with Chief Secretary.

The usual monthly discussions with the Chief Secretary have taken place throughout the year under review. It is considered that these informal discussions have been of mutual benefit and, as Minister for Health, Mr. McEwin has always been most appreciative of any suggestions put forward by either the President or the Immediate Past President.

Katherine Bishop Harman Prize.

Advice has been received from the Parent Association that a member of the Branch, Dr. Charles Swan, has won a Katherine Bishop Harman Prize of a certificate and a cheque for £75 for his essay entitled "Rubella in Pregnancy as an Ætiological Factor in Congenital Malformation, Stillbirth, Miscarriage and Abortion". The Council tenders its sincere congratulations to Dr. Swan upon this achievement.

Honours to Members of the Branch.

The Council tenders its congratulations to the following members whose names appeared in the New Year Honours: Professor J. B. Cleland—created a Commander of the Most Excellent Order of the British Empire; Dr. E. A. H. Russell—created an Officer of the Most Excellent Order of the British Empire; Dr. C. E. C. Wilson has been promoted to grade of Knight of Grace in the Venerable Order of the Hospital of St. John of Jerusalem.

The report contains a brief summary of the activities of the Council throughout the year under review. Many other items have engaged the attention of Council when matters affecting the interests of members have been dealt with.

The office duties are increasing each year, and I would like to thank Mr. Dobbie and Mr. Ladyman for the able way in which they have conducted the secretarial work of the Branch.

In conclusion, I desire to thank individual members and members of Council for the loyal support which I have received during my term of office.

(Signed) ALLAN D. LAMPHEE,
President.

SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION (INCORPORATED).

Library Account.

	£ s. d.		£ s. d.
To Balance brought down, December 12, 1947 ..	84 17 8	By Library Subscriptions	289 12 6
„ University Grant	300 0 0	„ Balance, December 31, 1948	96 5 2
„ Depreciation	1 0 0		
	£385 17 8		£385 17 8

Balance Sheet as at December 31, 1948.

LIABILITIES.	£ s. d.	£ s. d.	ASSETS.	£ s. d.	£ s. d.
Sundry Creditors		121 7 5	Plant and Fittings, *less* Depreciation		59 10 2
Lister Oration Fund (invested in Savings Bank as *per contra*) ..		97 13 4	Delineascope, *less* Depreciation		4 10 0
British Medical Hall: Building Fund		603 13 2	Projector, *less* Depreciation		6 10 0
General Fund Account—			Lister Medals and Dies		2 0 0
Balance as at December 31, 1947	3,544 16 1		Medical Certificate Books		6 18 4
Surplus Income over Expenditure for Year	420 19 7		British Medical Hall Company, Limited—		
		3,965 15 8	299 £10 Shares at Cost		3,021 10 0
			Australasian Medical Publishing Company, Limited—		
			Debentures at Cost		430 0 0
			THE MEDICAL JOURNAL OF AUSTRALIA—		
			Debenture Account		69 8 1
			Sundry Debtors—		
			General		1 3 6
			British Medical Hall Company, Limited ..		153 14 5
			Library Account		96 5 2
			Subscriptions in Arrear		6 16 6
			Special Accounts—		
			Lister Fund—Savings Bank ..	£97 13 4	
			Library Account—Savings Bank	£1 14 10	
			Building Fund:		
			Savings Bank	£362 3 2	
			Commonwealth Bonds	£200 0 0	
					661 11 4
			Cash—		
			National Bank of Australasia ..	£51 14 8	
			Savings Bank of South Australia	£141 12 6	
			Commonwealth Savings Bank ..	£69 2 2	
			In Hand	£6 2 9	
					268 12 1
		£4,788 9 7			£4,788 9 7

F. C. W. DOBBIE, Secretary. PERCIVAL T. S. CHERRY, Honorary Treasurer.

AUDITORS' REPORT.

We hereby report we have examined the Books and Accounts, as produced to us, of the South Australian Branch of the British Medical Association (Incorporated) for the year ended December 31, 1948. In our opinion the above Balance Sheet is properly drawn up so as to exhibit a true and correct view of the affairs of the Branch as at the above date according to the best of our information, the explanations given us and shown by the books produced.

Adelaide,
May 12, 1949.

MUECKE, PICKERING AND COMPANY,
Chartered Accountants (Australia), Auditors.

SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION (INCORPORATED).

Income and Expenditure Account for the Year ended December 31, 1948.

	£	s.	d.
To British Medical Association, London	704	5	10
„ THE MEDICAL JOURNAL OF AUSTRALIA	339	18	9
„ Federal Council Capitation Fee	417	15	0
„ Library Subscriptions	289	12	6
„ Amount Written off Subscriptions	2	7	6
„ Postages and Telegrams	152	13	4
„ Stationery and Printing	193	15	7
„ Telephone	26	16	8
„ Rent	96	1	6
„ Salaries	908	0	0
„ Superannuation	66	6	8
„ Legal Expenses	8	18	6
„ Audit Fee	10	10	0
„ General Expenses	165	13	10
„ Surplus Income over Expenditure Transferred to General Fund Account	420	19	7
	£3,803	15	3

	£	s.	d.	£	s.	d.
By Subscriptions—						
City	2,810	4	6			
Country	944	2	3			
Accrued	6	16	6			
				3,761	3	3
„ Interest				36	2	5
„ Medical Certificate Books				5	13	3
„ Section of History					9	11
				£3,803	15	3

Financial Statement.

The financial statement, which is printed herewith, was adopted on the motion of Dr. P. T. S. Cherry, seconded by Dr. A. L. Tostevin.

Induction of President.

Dr. A. D. Lamphee inducted to the office of president for the year 1949-1950 Dr. C. O. F. Rieger and invested him with the badge of office. Dr. Rieger thanked the members for his election.

Election of Office-Bearers.

Dr. Rieger announced the election of the following office-bearers for the forthcoming year:

Vice-President: Dr. G. H. Burnell.
Honorary Treasurer: Dr. F. L. Wall.
Honorary Medical Secretary: Dr. R. F. West.
Members of Council: Dr. M. E. Chinner, Dr. R. H. Hamilton, Dr. F. B. Turner, Dr. R. C. Heddle.

Messrs. Muecke, Pickering and Company were elected auditors for the ensuing year.

The Retiring Treasurer.

On the motion of Dr. John Verco, a vote of thanks was recorded to Dr. P. T. S. Cherry, the retiring honorary treasurer. Dr. Cherry had served on the Council for eighteen years and had been honorary treasurer continuously for the last eleven years. During his long service on the Council he had held the offices of vice-president and president.

The Retiring Members of Council.

On the motion of Dr. E. F. West, seconded by Dr. C. H. Schafer, a vote of thanks was recorded to the retiring members of Council—Dr. L. L. Davey, Dr. S. J. Douglas, Dr. J. Estcourt Hughes and Dr. G. Wien Smith.

Retiring President's Address.

Dr. A. D. Lamphee read his retiring president's address entitled "The Changing Face of Medicine" (see page 865).

Dr. H. M. J. Halloran proposed and Dr. E. F. Gartrell seconded a vote of thanks to Dr. Lamphee for his address. The vote was carried by acclamation and Dr. Lamphee replied.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on October 18, 1949, at the Victorian Eye and Ear Hospital, East Melbourne. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital.

Morgagnian Cataract with Absorption of Cortex.

DR. A. S. ANDERSON showed a female patient, aged sixty-two years, who had presented herself at the hospital on June 29, 1949, with acute glaucoma of the right eye, which was thought to be of primary character until it was found that she had been examined in 1940 when she had an immature cataract and keratic precipitates in that eye. A further attack occurred on July 31, and on August 8, when the attack had subsided, an anterior sclerectomy with glaucoma iridectomy was performed. The vision in the right eye was then the perception of hand movements. Post-operatively the lens nucleus could be seen moving under the influence of gravity in a fluid cortex containing cholesterin crystals. Keratic precipitates were present in abundance and were of gelatinous type. On October 17 the fluid cortex had been absorbed, and the visual acuity with a cataract lens was $^{6}/_{12}$.

Chronic Glaucoma with Dilated Scleral Veins.

Dr. Anderson then presented a female patient, aged sixty-five years, who had attended the out-patient department complaining of redness of the eyes, which had been present for two years. Examination revealed great dilatation of the subconjunctival vessels of both eyes. There were early lens opacities and pigmentary degeneration of the macula of the right eye. The optic disks were normal. The visual acuity in the right eye was $^{3}/_{60}$, and this could not be improved. The visual acuity in the left eye after correction with a convex sphere of 2·5 dioptres and a convex cylinder of 0·25 dioptre with an axis of 90° was $^{6}/_{5}$. The visual field in the left eye was full to $^{5}/_{330}$ (white object); in the right eye there was marked loss to within 10° of the fixation point above and in the lower nasal quadrant. The intraocular tension had been watched at regular intervals since July 11, 1949, when it was 35 millimetres of mercury (Schiotz). The patient had been kept under treatment with pilocarpine and eserine drops, and the tension at the time of the meeting was 24 millimetres of mercury in the right eye and 30 millimetres in the left.

Recurrent Corneal Ulceration.

Dr. Anderson's last patient was a woman, aged sixty years, who had attended at the out-patient department on March 21, 1949, with an ulcer at the lower temporal margin of the cornea of the left eye. The ulcer was treated along the usual lines, but was followed by recurrences. A lateral tarsorrhaphy was performed on September 15. The patient had a dense leucoma of the periphery of the left cornea and a mild degree of *acne rosacea* of the face. The right cornea was normal. The condition was thought possibly to be rosacea keratitis.

Vitreous Hæmorrhage possibly Eales's Disease.

DR. NORMAN GEANEY showed a male patient, aged thirty-one years, who complained of blurred vision for six weeks in the right eye; the condition had become much worse in the past few days. Examination revealed multiple vitreous opacities in the right eye and details of the *fundus oculi* could not be determined; no keratic precipitates were present. The left eye was normal. Investigations had been commenced, but no results were to hand. The diagnosis was vitreous hæmorrhage possibly Eales's disease.

Lymphomatosis of the Lids.

DR. W. L. DUNCAN presented a male patient, aged forty years, who had attended the out-patient department on June 7, 1949, and stated that the right lower lid had been swollen for ten days. Examination revealed that there was much bulging of the fornices of the upper and lower lids of both eyes, but that of the right lower lid was the greatest. The result of a Wassermann test was negative. The results of blood cell counts were within normal limits. X-ray examination of the chest did not reveal any pulmonary abnormality or enlargement of mediastinal glands. Smear and cultural examination of the conjunctival sacs revealed a normal cell content and normal flora. Biopsy of tissue

from the right lower fornix revealed lymphoid hyperplasia. The patient had had deep X-ray therapy, and slight improvement had occurred.

Retinitis Pigmentosa.

Dr. Duncan next showed a man, aged twenty years, with a visual field reduced to 5° from the fixation point in both eyes and a typical fundal picture of *retinitis pigmentosa*. No family history of blindness or visual defect was elicited, but there was consanguinity of the parents. The result of a Wassermann test was negative.

Dr. E. D. O'Brien also showed a male patient, aged twenty-four years, in whom night blindness had been noted at the age of thirteen years. Loss of the peripheral field was well marked at the age of sixteen years, when the field extended to 5° from the fixation point in both eyes. No significant family history in three generations was elicited. Right cervical sympathectomy was performed in May, 1942. The visual acuity was $^6/_9$ with correction in each eye. The visual field was limited to within 4° of the fixation point. Typical *retinitis pigmentosa* was seen on examination of the *fundus oculi*.

Posterior Staphyloma.

Dr. Duncan's third patient was a woman, aged thirty-one years, who had presented with acute conjunctivitis in both eyes and stated that the right eye had always been weak. The visual acuity in the right eye was ability to count fingers and in the left eye was $^6/_4$. Examination of the *fundus oculi* showed a large area on the temporal side of the optic disk, which was highly myopic and in which the retina and chorioid were atrophied to show a white area of sclera across which ran a few large chorioidal vessels. The affected area was sharply demarcated from the normal part of the retina.

Nævus of the Upper Lid.

Dr. Duncan then showed a female patient, aged eighteen months, who had been brought to the out-patient department on July 22, 1949, with the history that the skin in the region of the left inner canthus was discharging. There was a swelling at the inner angle of the left upper lid. There was no regurgitation of fluid from the lachrymal sac, and no pus was seen. X-ray examination of the bony orbit revealed no abnormality. The mother reported on November 23, 1948, and March 1, 1949, that the swelling varied in size. The nature of the swelling was discussed, and it was thought that a nævus was the most probable diagnosis.

Thrombosis of Central Retinal Vein.

Dr. Duncan's fifth patient was a woman, aged sixty-six years, who had sought advice on October 11, 1949, and stated that the left eye had become blind during the previous week. The patient had suffered from high blood pressure for thirteen years. The left eye contained massive retinal hæmorrhages, most marked along the vessels. The retinal vessels of the right eye showed moderate arteriosclerotic changes. The blood pressure was 225 millimetres of mercury (systolic) and 110 millimetres (diastolic), but there was no evidence of cardiac or renal failure.

Senile Cataract.

Dr. Duncan's last patient was a woman, aged ninety-one years, who had attended the hospital because of failing vision in both eyes. Examination revealed mature cataract in both eyes.

Papillœdema of Undetermined Ætiology.

DR. E. D. O'BRIEN presented a male patient, aged thirty-nine years, who had attended the hospital on October 30, 1949, because hot solder had splashed into the right eye the day previously. For three weeks prior to the date of attendance he had suffered from severe headaches which lasted throughout the day. There had been no vomiting. The right cornea did not stain with fluorescein, but there was a burn of the right lower lid. The visual acuity in his right eye was $^6/_{18}$; this was improved to $^6/_5$ with a convex cylinder of 1·75 dioptres with an axis of 90°. The visual acuity in the left eye was $^6/_6$, improved to $^6/_5$ with a convex sphere of 0·25 dioptre and a convex cylinder of 1·0 dioptre with an axis of 90°. Both optic disks were swollen approximately two dioptres with blurring of the upper and nasal margins, but no hæmorrhages, exudate or retinal œdema could be detected in either eye. The blood pressure was 180 millimetres of mercury (systolic) and 115 millimetres (diastolic). Systemic examination otherwise revealed no abnormality. Urine examination and renal function tests yielded normal findings. X-ray examination of the skull showed no abnormality, and evidence of increased intracranial pressure was absent. The visual fields were full to $^3/_{330}$ (white object) and the blind spots were not enlarged to $^1/_{1000}$ (white object). The patient was still under observation. It was suggested that the condition was mild virus encephalitis.

Orbital Tumour with Recurrence in Skin Flap.

DR. KELVIN LIDGETT presented a girl, aged four years, who had been first brought for advice on May 21, 1949, with the history that six weeks previously the right eye had appeared to be smaller than the left eye. Examination revealed pronounced right proptosis and swelling of the outer part of the right upper lid. There was no enlargement of the regional lymph nodes, and the swelling was not tender. The visual acuity could not be estimated; the retina was normal. The X-ray appearance of the skull was normal. Deep X-ray therapy was given, but did not produce any retrogression of the proptosis. Repeated physical and X-ray examination did not reveal any primary tumour or metastasis. Exenteration of the orbit was performed on September 14, the greater part of the lids being used to form skin flaps. The orbit healed rapidly, the bare area being covered by a split-skin graft. On October 17 a swelling was noticed in the lower skin flap, which had increased rapidly in the last three days, and was now approximately half an inch in diameter at the time of the meeting. It was intended to excise the skin flaps.

Ocular Syphilis.

Dr. Lidget then showed a man, aged thirty-two years, who illustrated some of the ocular manifestations of syphilis. The condition was one of old interstitial keratitis which had left corneal opacities, disseminated chorioiditis, irregular pupils due to posterior synechiæ and vitreous opacities. The vision in the left eye was very defective, and the eye had become divergent.

(To be continued.)

Post-Graduate Work.

MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

MEDICAL POST-GRADUATE FACILITIES IN VICTORIA IN 1950.

THE following summary of medical post-graduate facilities which will be available in Melbourne and Victorian country centres in 1950 has been drawn up by the Melbourne Permanent Post-Graduate Committee.

Clinical Post-Graduate Week.

The honorary medical staffs of Saint Vincent's and the Children's Hospitals, Melbourne, will conduct a clinical post-graduate week, commencing on October 9, 1950, to be held on three days at Saint Vincent's Hospital and on two days at the Children's Hospital. There will be no charge for attendance.

Courses for General Practitioners.

Gynæcology and Obstetrics Refresher Course.

A gynæcology and obstetrics refresher course will be conducted by the Melbourne Permanent Post-Graduate Committee from August 14 to 25, 1950, at the Women's Hospital, Carlton. Residence at the hospital during the period is advised and will be available. Fees for tuition will be 10 guineas, and for residence £3 10s. per week.

Evening Lectures in Gynæcology and Obstetrics.

Evening lectures in gynæcology and obstetrics will be arranged by the State Committee of the Royal College of Obstetricians and Gynæcologists on alternate Wednesdays from July 5 to September 13, 1949, at the Women's Hospital, Carlton, at 8.30 p.m. Fees will be £2 2s. per course or 10s. 6d. per lecture.

Anæsthesia.

Individual practical training in anæsthesia can be arranged upon application to the Melbourne Permanent Post-Graduate Committee. The course can start at any time, extend over any required period and involve full-time or part-time study. It will consist of instruction in anæsthesia and the actual giving of anæsthetics under supervision at various Melbourne hospitals, but will not include courses of lectures. The fee will be at a fixed rate per week depending on the number of sessions.

Country Courses.

Throughout the year the Post-Graduate Committee will conduct a series of country courses, each consisting of three or four lecture-demonstrations. The following dates and places have been arranged: February 18 and 19, at Ballarat; March 25 and 26, at Mooroopna; April 1 and 2, at Sale; June 17 and 18, at Mooroopna; August 26 and 27, at Mildura; September 16 and 17, at Bendigo; October 7 and 8, at Horsham; November 18 and 19, at Mortlake.

In addition there will be several one-day courses at country centres. Fees are charged at the rate of 10s. 6d. per lecture. The first of these will be given by Dr. J. Eric Clarke at Portland on February 4, 1950, on "Non-Tuberculous Pulmonary Disease".

Overseas Lecturers.

Announcements of courses conducted by overseas lecturers will be made when arrangements permit.

Instruction in Poliomyelitis.

The Melbourne Permanent Post-Graduate Committee will arrange for members of the Consultative Council on Poliomyelitis visiting country centres to give instruction in poliomyelitis to practitioners in those districts, either by demonstration of patients or by lectures. Practitioners will be notified of any such arrangements.

Course at Flinders Naval Depot.

By arrangement with the Royal Australian Navy the Melbourne Permanent Post-Graduate Committee will conduct medical and surgical demonstrations at Flinders Naval Depot on the second Wednesday of each month in 1950, from February to September, except in July, and on the first Wednesday of October, November and December, all at 2.30 p.m.

Course in Psychiatry.

A course in psychiatry consisting of about ten lecture-demonstrations in common problems in psychological medicine occurring in general practice will be conducted in Melbourne during the latter part of 1950.

Study for Higher Qualifications.

The following courses will be suitable for candidates for higher qualifications conducted only if enrolments are sufficient in number in each case.

Part I Courses.

Courses in anatomy, physiology and pathology, suitable for candidates for Part I of examinations for the M.D., M.S., D.O., D.L.O., D.G.O., D.D.R., D.T.R.E., D.A. and D.P.M., will be held on Monday and Wednesday afternoons, and courses in physics for candidates for the D.D.R. and D.T.R.E. on Thursday afternoons. These will be conducted by the Melbourne Permanent Post-Graduate Committee at the University of Melbourne, the classes commencing on March 15, 1950, and continuing till August. The fee for Part I of each course is 30 guineas.

A course for candidates for the primary F.R.A.C.S. and F.R.C.S. examinations will be conducted by the Royal Australasian College of Surgeons, commencing on or about July 15, 1950.

Part II Courses.

Course for Candidates for M.D.II and M.R.A.C.P.—From February till early in August, 1950, the Melbourne Permanent Post-Graduate Committee will conduct clinical lecture-demonstrations dealing with medical problems, each under the direction of a senior specialist, with various clinicians taking part. The demonstrations are available to all registered medical practitioners, but are designed primarily for those preparing for higher qualifications. They will be given on two afternoons a week at different hospitals. The following courses have been arranged: Hæmatology, under the direction of Dr. J. A. McLean, February 2 to 21; fee, three guineas. Neurology, under the direction of Dr. E. Graeme Robertson, March 14 to 30; fee, three guineas. Thoracic diseases, under the direction of Dr. Clive Fitts, April 4 to 20; fee, three guineas. Pædiatrics, under the direction of Dr. Mostyn L. Powell, April 27 to May 16; fee, three guineas. Endocrinology, under the direction of Dr. Keith D. Fairley, May 18 to June 6; fee, three guineas. Cardiology, under the direction of Dr. Frank J. Niall, June 8 to 27; fee, three guineas. Gastro-intestinal disorders, under the direction of Dr. Ian J. Wood, June 29 to July 13; fee, £2 12s. 6d. Renal disorders, under the direction of Dr. Leslie Hurley, July 18 to August 3; fee, three guineas. Fees are at the rate of 10s. 6d. per demonstration.

A Course in Advanced Medicine.—A course in advanced medicine suitable for candidates for M.R.A.C.P. and M.D.II, but also open to all graduates, will be conducted by the Royal Australasian College of Physicians on three afternoons a week, for six weeks in each course, in February and March and in August and September. The course will be held at Prince Henry's Hospital, Melbourne, and the fee will be approximately £12 12s.

Surgery.—A course for candidates for the final F.R.A.C.S. examinations will be conducted by the Royal Australasian College of Surgeons from mid-January till the end of April, 1950. The fee will be 30 guineas.

Courses for Diploma Examinations.—Prior to the examinations and as the demand arises, the Melbourne Permanent Post-Graduate Committee will arrange courses suitable for candidates for Part II of the required diplomas. Candidates for such courses should make inquiries from the committee as early as they can. It will not be possible to attend all classes for Parts I and II of a diploma during the one year. Classes in basic pathology will commence on March 15, 1950, at the university. A course in bacteriology suitable for candidates studying for higher qualifications will commence on February 1, 1950, at 4.30 p.m. at the university, and will finish before the Part II diploma examinations in March. Two courses for candidates for the D.O. Part II will commence on January 16, 1950; the first will consist of lectures in medical ophthalmology by Dr. G. Brew, Dr. A. Joyce and Dr. J. Billings, lectures in operative surgery by Dr. W. Box and clinical lectures by the honorary medical staff of the Eye and Ear Hospital; the second will consist of lectures in pathology by Dr. K. O'Day and Dr. Hugh Ryan. Individual practical training in anæsthesia can be arranged for candidates for the D.A. Part II upon application to the Post-Graduate Committee; the course can start at any time, extend over any required period and involve full-time or part-time study; it will consist of instruction in anæsthesia and the actual giving of anæsthetics under supervision at various Melbourne hospitals, but will not include courses of lectures.

Psychological Medicine.—A full-time course in psychological medicine, arranged in consultation with the Australasian Association of Psychiatrists, will be conducted in Melbourne in August.

Obstetrics and Gynæcology.—A course suitable for candidates for the M.R.C.O.G. and D.G.O. Part II will be conducted by the Victorian State Committee of the Royal College of Obstetricians and Gynæcologists, commencing on August 1 and continuing till about the end of September, 1950.

Individual Post-Graduate Clinical Study.

With due notice the Melbourne Permanent Post-Graduate Committee can arrange attendances at general or special clinics, singly or as a series, to meet individual needs. Information concerning the visiting and operating days of members of hospital staffs and daily operating lists are kept by the Post-Graduate Committee.

Special arrangements for attendances at clinics can be made at the Austin Hospital, Heidelberg, for those interested in the medical or surgical treatment of tuberculosis, in the treatment of cancer by surgery or radium implantation, or in orthopædic surgery.

Fees are £1 1s. for enrolment and £1 1s. per week of attendance, or *pro rata* for part-time attendance.

Regular Meetings of Clinical Societies and Other Medical Bodies.

Throughout the year regular clinical meetings are conducted. Attendance at these is by invitation, and details may be obtained from the respective hospitals or societies, or from the Melbourne Permanent Post-Graduate Committee.

Examinations.

Information concerning examinations held in Victoria should be obtained from the examining bodies themselves.

Application for Courses.

Application for courses, accompanied by any fees payable, should be made to the secretary of the organization by which the course is to be conducted.

Addresses.

Addresses of those conducting the courses set out above are as follows:

The Melbourne Permanent Post-Graduate Committee, 426 Albert Street, East Melbourne, C.2. Cables: "Postgrad", Melbourne. Telephone: JM 1547.

The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney, N.S.W. The Victorian Secretary is Dr. J. Eric Clarke, 12 Collins Street, Melbourne. Telephone: JM 1324.

The Royal Australasian College of Surgeons, Spring Street, Melbourne. Cables: "Collsurg", Melbourne. Telephone: JA 2002.

The Victorian State Committee of the Royal College of Obstetricians and Gynæcologists. Secretary: Dr. W. J. Rawlings, 12 Collins Street, Melbourne. Telephone: JM 1375.

Inquiries regarding the Clinical Post-Graduate Week should be made to the secretary of the honorary medical staff of Saint Vincent's Hospital, Victoria Parade, Fitzroy, or of the Children's Hospital, Pelham Street, Carlton.

University Examinations.

Inquiries concerning university examinations should be addressed to the Registrar, University of Melbourne, Carlton, N.3, Victoria. Candidates, if in Melbourne, will find it more convenient to make an appointment with the Secretary of the Faculty of Medicine, Scientific and Medical Branch of the Registrar's office.

The Royal Australasian College of Physicians.

COUNCIL MEETING.

A MEETING of the Council of The Royal Australasian College of Physicians was held at Melbourne on November 10 and 11, 1949. An examination for membership of the College was also held.

Admission of Members.

The following candidates who were successful at examinations held in Australia and New Zealand were admitted to membership of the College: Dr. S. P. Bellmaine, Dr. W. J. Burke, Dr. E. G. McQueen, Dr. T. I. Robertson and Dr. John H. Tyrer, of New South Wales; Dr. I. S. Epstein, Dr. K. H. Heard, Dr. C. J. McRae, Dr. Luke Murphy, Dr. G. B. Westmore and Dr. L. C. Hudson, of Victoria; Dr. B. S. Hetzel and Dr. C. C. Jungfer, of South Australia; and Dr. L. S. Antonoff-Lewis, of New Zealand.

The Archibald Watson Memorial Lecture.

The second Archibald Watson Memorial Lecture was delivered under the auspices of the College in the lecture hall of the Royal Australasian College of Surgeons by Professor J. B. Cleland on November 11, 1949. The lecture, which bore the title "The Naturalist in Medicine", will be published in this journal at a later date.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 92, of December 1, 1949.

AUSTRALIAN MILITARY FORCES.

Royal Australian Army Medical Corps.

VX65418 Captain (Temporary Lieutenant-Colonel) R. W. E. Hoyling relinquishes the temporary rank of Lieutenant-Colonel and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (3rd Military District), 7th July, 1949.

Citizen Military Forces.

Northern Command: Second Military District.

Royal Australian Army Medical Corps (Medical).—2/146556 Captain A. G. Finley is appointed from the Reserve of Officers, 2nd September, 1949.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 26, 1949.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.[2]	Australia.[2]
Ankylostomiasis	•	..	..	..	•	..	..	..	..
Anthrax	•	..	..	..	..	..	..	..	..
Beriberi	•	•	•	•	•	•	..	•	..
Bilharziasis	•	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	1	4(3)	..	..	1	..	..	..	6
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	•	•	•	•	•	•	•	•	..
Dengue	•	•	•	•	•	•	..	•	..
Diarrhœa (Infantile)	..	..	10(10)	..	..	..	..	..	10
Diphtheria	6(3)	5(4)	4(1)	1(1)	3(2)	..	..	..	19
Dysentery(*b*)	•	..	1(1)	..	..	..	..	..	1
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	•	•	•	..	•	•	..	..	..
Filariasis	•	..	..	..	..	..	..	..	..
Helminthiasis	•	..	•	•	•	•	•	•	..
Hydatid	•	..	•	•	..	•	..	..	..
Influenza	•	•	•	..	•	•	..	•	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*c*)	•	(*c*)	1(*c*)	(*c*)	(*c*)	(*c*)	(*c*)	(*c*)	1(*c*)
Measles	•	•	•	36(12)	•	•	..	..	36
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	6(3)	15(4)	1(1)	48(36)	..	3(1)	..	..	73
Psittacosis	•	..	•	..	•	•	•	•	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella(*h*)	•	•	5(3)	•	10	1(1)	..	..	16
Scarlet Fever	45(28)	26(8)	4(3)	4(1)	8(8)	1(1)	..	..	88
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	•	..	..	•	•	•	•	•	..
Trachoma	•	..	..	•	•	•	•	•	..
Tuberculosis(*d*)	25(19)	14(12)	2(2)	9(6)	4(3)	2(1)	..	..	56
Typhoid Fever(*e*)	..	..	..	..	..	..	..	..	..
Typhus (Endemic)(*f*)	..	..	1	..	..	..	..	..	1
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	•	•	1	•	•	•	•	•	1
Whooping Cough	•	•	•	35(10)	•	•	..	..	35
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 36, 1944–1945. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from Northern Territory and Australian Capital Territory.
• Not notifiable.
(*a*) Includes "Mossman" and "Sarina" fevers. (*b*) Includes amœbic and bacillary. (*c*) Statistics inexact with varying practice with regard to relapses in Service cases infected overseas. (*d*) Includes all forms except in Northern Territory, where only pulmonary tuberculosis is notifiable. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Cases reported include scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease. (*h*) Notifiable disease in Queensland in females aged over fourteen years.

Southern Command: Fourth Military District.

Royal Australian Army Medical Corps (Medical).—4/31910 Captain R. D. Hammill is transferred to the Reserve of Officers (Royal Australian Medical Corps (Medical)) (4th Military District), 17th August, 1949. To be Captain (provisionally), 7th September, 1949: 4/31955 Harold Robinson Moore.

Western Command: Fifth Military District.

Royal Australian Army Medical Corps (Medical).—5/32057 Major R. G. Linton is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (5th Military District), 1st September, 1949.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

1st Military District.—To be Honorary Captain, 7th September, 1949: Ross Leonard Green.

3rd Military District.—Captain T. G. B. Allen is retired at his own request, 20th August, 1949. The resignation of Captain J. N. Diggle of his commission is accepted, 9th May, 1949. To be Honorary Captain, 13th September, 1949: Graham Windham Cooper.

4th Military District.—The following officers are placed upon the Retired List (4th Military District) with permission to retain their rank and wear the prescribed uniform, 8th August, 1949: Lieutenant-Colonel (Honorary Colonel) F. N. Le Messurier, D.S.O., Lieutenant-Colonel J. S. Verco, Major E. E. Broadbent and Captains H. F. Dunstan and E. F. Pflaum.

7th Military District.—To be Major, 7th September, 1949: Moses Sendak, O.B.E.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

Evans, Cyril Percival Victorious, M.B., B.S., 1943 (Univ. Sydney), D.T.M., 1946 (Univ. Sydney), Scottsdale, Tasmania.

Cooper, Desmond Albert, M.B., B.S., 1949 (Univ. Melbourne), Hobart.

Fleming, William Brian, M.B., B.S., 1949 (Univ. Melbourne), Burnie.

Grove, Barry Rutherford, M.B., B.S., 1949 (Univ. Melbourne), Launceston.

Wood, Ian Hadley, M.B., B.S., 1949 (Univ. Melbourne), Launceston General Hospital, Launceston.

Obituary.

HENRY BUDD HETHERINGTON.

WE regret to announce the death of Dr. Henry Budd Hetherington, which occurred on December 5, 1949, at Moss Vale, New South Wales.

HERBERT ODILLO MAHER.

WE regret to announce the death of Dr. Herbert Odillo Maher, which occurred on December 5, 1949, at Double Bay, New South Wales.

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Burdon, Kenneth Ray, M.B., B.S., 1949 (Univ. Adelaide), 10 Fisher Street, Tusmore.

Bennett, John Barkley, M.B., B.S., 1947 (Univ. Adelaide), 19 Fullarton Road, Fullarton.

Hicks, Neil Dennis, M.B., B.S., 1948 (Univ. Adelaide), 11 Grandview Grove, Toorak Gardens.

The undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Kalokerinos, James, M.B., B.S., 1948 (Univ. Sydney), 560 Old South Head Road, Rose Bay, New South Wales.

Diary for the Month.

JAN. 4.—Western Australian Branch, B.M.A.: Council Meeting.
JAN. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JAN. 10.—New South Wales Branch, B.M.A.: Council Quarterly.
JAN. 12.—South Australian Branch, B.M.A.: Council Meeting.
JAN. 14.—Queensland Branch, B.M.A.: Council Meeting.
JAN. 17.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JAN. 25.—Victorian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135 Macquarie Street, Sydney): Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester United Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Austr lia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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